

EFFECT OF 6 MONTHS OF EXERCISE TRAINING ON CARDIOVASCULAR
AND HORMONAL RESPONSES TO HEAD UP TILT IN ELDERLY MEN
AND WOMEN

BY

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This work is dedicated to my parents who always believed in me, and to my husband, who helped me accomplish my goals.

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By

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To evaluate the effect of 6 months of exercise training on heart rate, stroke volume (SV), cardiac output (\dot{Q}), blood pressure, and hormonal responses to head-up tilt (HUT), 22 women and 11 men (60 to 82 years) were assigned to treadmill exercise (TREAD; n = 14), treadmill plus resistance exercise (TREAD/RESIST; n = 10), or non-exercising control (n = 9) groups. Tilt testing before (T1) and after (T3) training consisted of 30 minutes of supine rest, 15 minutes of 70° HUT, and 15 minutes of supine recovery. Plasma volume (PV), aldosterone (ALDO), vasopressin (AVP), adrenocorticotrophic hormone (ACTH), plasma renin activity (PRA), norepinephrine (NE), epinephrine (EPI), sodium (Na⁺), potassium (K⁺), and

protein (PROT) were measured after 30 minutes of supine rest. Hormones were also measured after 15 minutes of HUT.

Training increased maximal aerobic power in TREAD and TREAD/RESIST by 16.4% and 13.7%, respectively ($p \leq 0.05$). TREAD decreased body weight and skinfold measurements while TREAD/RESIST increased elbow flexion and extension strength ($p \leq 0.05$).

Resting SV and \dot{Q} increased 20.6% and 13.4%, respectively, in TREAD ($p \leq 0.01$); resting \dot{Q} decreased 9.1% in TREAD/RESIST ($p \leq 0.05$). Average tilt test SV and \dot{Q} increased 15.0% and 9.3%, respectively, in TREAD; average test \dot{Q} decreased 9.8% in TREAD/RESIST ($p \leq 0.05$). The combined training group increased PV by 9.5%, while resting plasma levels of ACTH, AVP, ALDO, K^+ , Na^+ , PROT, NE, and EPI were not changed with training. Four subjects experienced presyncopal symptoms at T1 associated with large increases in ACTH and AVP. Improved responses at T3 may be related to increased SV and \dot{Q} .

The results suggest a) endurance training increases resting and orthostatic SV and \dot{Q} , while endurance plus resistance training decreases resting and orthostatic \dot{Q} . The difference between training groups may be related to changes in PV and venous return; b) PV increases with training in the elderly but resting hormonal levels are unchanged, suggesting a change in the stimulus-response relationship between blood volume and hormone secretion via volume sensitive cardiopulmonary receptors; c) training improves responses of older, intolerant subjects to tilt, mediated by increased SV and \dot{Q} .

CHAPTER 1 INTRODUCTION

Changing demographics in the United States in the latter half of the 20th and into the early 21st century indicates that persons over the age of 65 comprise the fastest growing segment of the population. In 1980, 11% of the population was over the age of 65 but this proportion is expected to increase to 18% by the year 2030 (Abrams & Berkow, 1990). When the elderly population is further delineated, it can be seen that the oldest group in our society (85+ years) has increased by 24.8% since 1980. During this period, the 75-84 year old group grew 17.1% while the 65-74 year old group increased by 11%. In absolute numbers, there are expected to be 34.9 million elderly by the year 2000, an increase of 17.1% over 1987 (Beck, 1989). Thus, an understanding of the physiological changes associated with aging and how these changes impact on homeostatic responses in older persons takes on a great deal of importance.

Changes in the cardiovascular system that are associated with aging may predispose older individuals toward disorders of blood pressure (BP) control mechanisms. Acute BP changes are buffered by the high-pressure carotid and aortic baroreflex system. In the elderly, an attenuation of baroreflex sensitivity has been attributed to a decrease in arterial compliance, which results in a decreased deformation of the baroreceptors during a given pressure change (Lipsitz, 1990) and thus an attenuated afferent signal. There may also be a decrease in the efferent baroreceptor-mediated responsiveness of heart rate (HR) acceleration during hypotensive stimuli (Gribbin, Pickering, Sleight, & Peto, 1971; Lipsitz, 1990). A decrease in cardiac compliance in the elderly is another

aging change that limits the ability of the senescent heart to increase end-diastolic volume (EDV) and/or decrease end-systolic volume (ESV); this results in a decreased ability to compensate for declines in cardioacceleration capacity by way of an increase in stroke volume (SV) (Shannon, Maher, Santinga, Royal, & Wei, 1991). Finally, either a decrease in β -receptor sensitivity in the peripheral vasculature or a decrease in vascular compliance may lead to diastolic BP or peripheral resistance responses to orthostasis that are not easily modified (Sowers, 1987).

The neuroendocrine system is also altered with age. There is a decrease in the secretory rate and plasma concentration of aldosterone when sodium intake is unrestricted; there is also a decline in aldosterone secretion in response to sodium restriction (Gregerman & Bierman, 1981; McGinty, Stern, & Akshoomoff, 1988). This decline parallels the decline in basal levels of renin activity. Although vasopressin levels may not be affected by aging, the ability of the kidney to concentrate urine is decreased due to a decrease in glomerular filtration rate rather than to a decrease in sensitivity to vasopressin. These changes might be expected to decrease the body's ability to augment plasma volume (PV) with endurance training. Vasoconstrictive responses may also be affected: although there is an increase in plasma norepinephrine concentration with age, there is a diminished vascular contractile response (Gregerman & Bierman, 1981; McGinty et al., 1988). This, together with the decrease in renin activity, may affect the ability of the senescent vasculature to adequately respond to hypotensive stimuli.

One manifestation of aging changes is the presence of orthostatic (postural) hypotension. In their review, Robbins and Rubenstein (1984) estimate that approximately 20% of those over age 65 have postural hypotension and that the prevalence in persons over age 75 may exceed 30%. Lipsitz (1990) also

estimates a 20 to 30% rate of postural hypotension in the noninstitutionalized elderly. These rates, however, may reflect the presence of risk factors associated with postural hypotension (hypertension, varicose veins, central nervous system disorders, certain medications); the presence of postural hypotension in the healthy elderly may be lower than this (Dambrink & Wieling, 1987; Mader, Josephson, & Rubenstein, 1987).

In younger populations, there have been both cross-sectional and longitudinal studies that have sought to determine the factors associated with orthostatic intolerance and the best training regimen to improve the responses to orthostasis. A training-induced hypervolemia has been hypothesized as a mechanism for improving cardiovascular responses to an orthostatic stress. Convertino, Montgomery, and Greenleaf (1984) found that a decrease in the HR and rate-pressure product responses to a 60° head-up tilt after 8 days of cycle ergometer training correlated significantly ($r = -0.68$) with a training-induced increase in blood volume. Similarly, Shvartz, Convertino, Keil, and Haines (1981) found that improvement in tilt tolerance and a decreased HR response to head-up tilt after training was related to an increased PV.

An increase in muscle mass is another mechanism hypothesized to help improve responses to orthostasis. According to this theory, an increase in muscle mass or tone limits venous pooling during orthostasis and thus better maintains venous return, cardiac output (\dot{Q}), and arterial pressure. Support for this theory was provided by several studies showing that postural hypotension in response to simulated microgravity was associated with decreased musculature, particularly in the lower extremities, and increased compliance in the leg vasculature (Convertino, Doerr, Mathes, Stein, & Buchanan, 1989; Duvoisin, Convertino, Buchanan, Gollnick, & Dudley, 1989). Two early training studies by Shvartz (1968a, 1969) also tend to lend support to this theory. In 1968, Shvartz

found that 3 months of gymnastic training on "heavy apparatus" was superior to volleyball and general conditioning for improving the systolic BP and pulse pressure response to a 10-minute standing test. It was hypothesized that an increase in abdominal muscle strength in the gymnastics group could explain the results; however, abdominal strength was not measured. In the later study (1969), Shvartz found that a 7-week program of upper body resistance-type exercises was superior to a program of bench-stepping for improving the systolic BP and pulse pressure response during head-up tilt. This appeared to indicate that some mechanism involved in the adaptation to resistance training was responsible for the improvement, but no explanatory mechanisms were offered by the author.

A third mechanism proposed to improve responses to orthostasis is an increase in baroreceptor responsiveness. This refers to the HR increment resulting from a given arterial pressure decrement. Several recent cross-sectional studies have compared the baroreceptor response of weightlifters and endurance-trained subjects to lower body negative pressure and/or a phenylephrine infusion (Smith, Graitzer, Hudson, & Raven, 1988; Smith & Raven, 1986). Both investigations have found that the peripheral resistance response of the two groups was similar and concluded that the more effective maintenance of BP in the weight-trained individuals was due to an enhanced baroreceptor sensitivity. Weight training may therefore play a role in improving responses to orthostasis either by increasing baroreceptor responsiveness and/or by increasing muscle mass.

Finally, altered neuroendocrine secretion or altered vascular sensitivity to pressor hormones may affect responses to orthostasis. Although most cross-sectional and longitudinal studies do not find that training changes the resting plasma levels of vasopressin and renin (Freund, Claybaugh, Hashiro, & Dice,

1988; Convertino, Brock, Keil, Bernauer, & Greenleaf, 1980; Convertino, Keil, & Greenleaf, 1983; Convertino, Mack, & Nadel, 1991; Wade, Dressendorfer, O'Brien, & Claybaugh, 1981), norepinephrine often decreases (Hagberg, Montain, Martin, & Ehsani, 1989b; Kiyonaga, Arakawa, Tanaka, & Shindo, 1985; Tipton, 1991). This is thought to reduce BP responses through decreases in HR and \dot{Q} . Altered vascular sensitivity to pressor hormones, in particular an increased β -adrenergic receptor sensitivity, may also play a role in altering responses to orthostasis after training (Wiegman, Harris, Joshua, & Miller, 1981; Wiegman, 1981).

Whether physical training can improve the responses to an orthostatic stress in the elderly is not known. Some of the components involved in the reflex responses to orthostasis may be irreversibly altered in the elderly (e.g., aortic distensibility, β -adrenergic sensitivity, cardiac and vascular compliance). In the young, an improved response to tilt after training consists of a decrease in HR and rate-pressure product associated with an increase in PV (Convertino et al., 1984; Shvartz et al., 1981). However, in the elderly, the HR and systolic BP responses to tilt are already attenuated (Dambrink & Wieling, 1987; Jansen, Lenders, Thien, & Hoefnagels, 1989; Kenny, Lyon, Bayliss, Lightman, & Sutton, 1987), due possibly to a decrease in the sensitivity of the baroreflex response (Gribbin et al., 1971). An improved response to tilt in the elderly after training may therefore involve increases, rather than decreases, in HR or systolic BP. It is possible that an increase in muscle mass after training would increase the systolic BP response to tilt through an improved venous return and SV. However, there may be a limit to the effect of this mechanism due to a decrease in left ventricular compliance in the elderly (Shannon et al., 1991). Blood pressure responses may also be limited by the decreased responsiveness of the vasculature to vasoactive hormones such as norepinephrine (Gregerman & Bierman, 1981; McGinty et al.,

1988). Finally, there may be a limit to the role that increased PV can play in the improvement in venous pressure because of impaired renal sodium conservation in the elderly (Gregerman & Bierman, 1981; Mader, 1989).

Based on the data from investigations with younger subjects, it appears that promising modes of training for the improvement in orthostatic responses are either weight training (Shvartz, 1968a, 1968b, 1969; Smith et al., 1988; Smith & Raven, 1986), or endurance training with a resistive component, such as cycling (Convertino et al., 1984; Greenleaf, Brock, Sciaraffa, Polese, & Elizondo, 1985; Shvartz et al., 1981) or uphill treadmill walking. Endurance exercise training with a resistive component for the elderly would combine some of the advantages of endurance and resistive training alone while eliminating some of the disadvantages. Endurance exercise training can improve aerobic capacity ($\dot{V}O_2\text{max}$) in the elderly an average of 15-30% (Adams & deVries, 1973; Hagberg et al., 1989b; Meredith et al., 1989; Seals, Hagberg, Hurley, Ehsani, & Holloszy, 1984). It can also cause a beneficial change in body composition (Graves, Panton, Pollock, Hagberg, & Leggett, unpublished), and a decrease in resting BP (Cononie et al., 1991; Hagberg, 1990; Hagberg & Seals, 1987), particularly in those who are hypertensive (Hagberg, Montain, & Martin, 1987; Hagberg et al., 1989b). Finally, endurance training is associated with increases in PV (Convertino et al., 1984; Oscai, Williams, & Hertig, 1968; Shvartz et al., 1981) although this effect has not been verified in older subjects.

One disadvantage of endurance training in the elderly is that elderly women appear to be more susceptible than elderly men to orthopedic injury related to high impact endurance activities such as jogging and fast walking (Pollock et al., 1991; Carroll et al., in press). Uphill treadmill walking, which provides a resistive component to the gluteal and hamstring muscles, but which allows a slower walking cadence and thus a reduction in impact forces, seems to

reduce injury occurrence in the elderly while providing an adequate stimulus for an increase in aerobic capacity (Hagberg et al., 1989a) and an increase in leg strength (Pollock et al., 1991). It is possible that muscle atrophy in the sedentary elderly is marked and that uphill treadmill walking would provide enough stimulus to improve muscular strength and thus improve the cardiovascular responses to orthostasis through enhanced venous return.

Resistance training induces increases in muscular strength in the elderly (Fiatarone et al., 1990; Frontera, Meredith, O'Reilly, Knuttgen, & Evans, 1988; Kauffman, 1985; Perkins & Kaiser, 1961) and may be beneficial in ameliorating the effects of decreased muscle mass on postural hypotension. Resistance training may also improve responses to orthostasis by an increase in baroreceptor sensitivity (Smith et al., 1988; Smith & Raven, 1986). A training program combining resistance training and uphill walking may therefore provide optimal fitness and health benefits while minimizing injuries.

Statement of the Problem

Most researchers investigating the effect of training on orthostatic responses have used young to middle-aged populations (Beetham & Buskirk, 1958; Convertino et al., 1984; Greenleaf et al., 1985; Greenleaf et al., 1988; Shvartz et al., 1981). No research has been conducted to date to determine whether any form of physical training can help improve the responses to an orthostatic challenge in the elderly. Consequently, different types of training programs using elderly subjects need to be conducted.

The specific aims of this research are a) to describe the cardiovascular and endocrine responses of elderly individuals to a 70° head-up tilt before and after 6 months of either uphill treadmill walking or a combination of uphill treadmill walking plus selected resistance training exercises; b) to determine whether

uphill walking or a combination of uphill walking plus selected resistance training exercises can improve the cardiovascular responses of elderly individuals to a 70° head-up tilt; and c) if orthostatic responses improve, to evaluate the mechanisms involved in the improvement.

Research Hypothesis

It is hypothesized that uphill treadmill walking of an intensity sufficient to induce significant changes in aerobic capacity and/or resistance training of an intensity to increase muscular strength of the arms and legs will result in positive adaptations in the cardiovascular responses to an orthostatic stress (70° head-up tilt). It is also hypothesized that one or more of the following training adaptations will correlate with the adaptations in orthostatic responses: increased lower body muscle mass and/or strength, an increased PV, increased baroreceptor responsiveness, and/or changes in pressor hormone secretion.

Justification

The increase in the elderly population in the United States and the increased cost of medical and pharmacological intervention to ameliorate the effects of aging underlines the importance of less costly interventions in the treatment of aging manifestations. In younger populations, there have been some promising results indicating that exercise training can improve the cardiovascular responses to orthostatic stresses (Convertino et al., 1984; Greenleaf et al., 1985; Shvartz 1968a, 1969; Shvartz et al., 1981). Yet the effect of exercise training on orthostatic responses has not been investigated in older individuals. Exercise training in healthy elderly individuals may provide information about potential mechanisms by which orthostatic responses may be improved in this population. In future studies, these mechanisms can be

investigated in other populations of elderly, e.g., those with documented orthostatic hypotension. Ultimately, exercise training may prove to be an alternative treatment for physiologic (aging-related) occurrences of orthostatic hypotension.

Assumptions

1. All laboratory equipment will yield accurate, reliable results over the course of repeated testing.
2. Subjects will follow instructions given to them regarding food, drink, and drug intake prior to testing.
3. Subjects will follow instructions given to them regarding the maintenance of current lifestyle (e.g., diet and exercise) outside of the prescribed program.

Delimitations

The following delimitations were imposed:

1. Subjects were over the age of 60 years.
2. Subjects recruited were sedentary and free from cardiovascular, pulmonary, peripheral vascular, or orthopedic diseases, or conditions that would limit their full participation in an exercise program.
3. Subjects were not diabetic.
4. Subjects had resting systolic and diastolic BP less than 160/100.
5. Subjects were not taking anti-anginal or digitalis medication.
6. Subjects did not previously have a myocardial infarction, coronary artery bypass surgery, or percutaneous transluminal coronary angioplasty.
7. Subjects did not have any resting or exercise electrocardiogram abnormalities indicative of significant ischemia or high grade dysrhythmia.

8. Subjects had a normal HR and BP response to maximal treadmill testing.
9. Strenuous exercise was not allowed within 12 hours prior to most testing procedures; strenuous exercise was not allowed within 24 hours prior to tilt testing.
10. Subjects were at least 3 hours but not more than 12 hours post-prandial during testing sessions; no caffeine was consumed within 3 hours prior to any test.
11. No alcohol was consumed within 24 hours prior to testing.
12. Subjects took usual prescribed medications prior to testing.

Limitations

Major limiting factors included the following:

1. Forty-four elderly subjects (14 males, 30 females) volunteered to serve as subjects.
2. Diet and day-to-day activity could not be regulated.

Definition of Terms

Aerobic exercise consists of activities that can be maintained continuously and involve rhythmic movement of large muscle groups. Aerobic activities, such as walking, jogging, running, swimming, cycling, and rope-skipping, are used to improve cardiorespiratory function.

Baroreflex responsiveness refers to the magnitude of the HR change in response to a given arterial pressure change. A decreased responsiveness refers to an attenuated HR response to a given pressure change.

Hypervolemia is an increase in blood volume.

Orthostasis is an environmental perturbation that produces qualitative effects similar to those induced by upright stationary posture (ConvertinoHR 1987).

Orthostatic (postural) hypotension is a reduction of 20 mmHg or more in systolic BP upon standing upright (Lipsitz, 1990).

Orthostatic intolerance is the inability of the cardiovascular reflexes to maintain arterial pressure for adequate cerebral blood perfusion, eventually leading to syncope (Convertino, 1987).

Resistance exercises consist of activities designed to increase muscular strength and/or endurance. These activities generally involve concentric and/or eccentric contractions of a muscle group against a constant or variable resistance and use free weights, and/or constant or variable resistance machines.

Syncope is synonymous with fainting.

CHAPTER 2 REVIEW OF LITERATURE

Introduction

The response to orthostasis involves an activation of reflex systems designed to maintain blood pressure (BP) homeostasis and cerebral perfusion despite the translocation of approximately 800 ml of blood from the central circulation to the periphery (Blomqvist & Stone, 1983). These reflexes include enhancement of myocardial function, increases in arterial and venous tone, increases in neuroendocrine secretion, and reflexes mediated by high- and low-pressure baroreceptors.

Endurance training in young individuals appears to be associated with alterations in some of the reflex responses to orthostasis. There may be a reduction in chronotropic responsiveness, and in the sensitivity of the high- and low- pressure baroreceptor systems. In addition, there may be an alteration in the sensitivity of vascular receptors, an increase in venous compliance, and an attenuation of vasoactive hormone release (Convertino, 1987). These changes would appear to compromise the body's ability to withstand an orthostatic challenge. On the other hand, training-induced adaptations that would appear to enhance the body's ability to withstand orthostasis include an increase in blood volume (BV) and an increase in muscle mass, particularly in the lower extremities.

The responses to orthostasis after endurance training in elderly persons have not been characterized. However, normal, healthy elderly persons demonstrate a quantitative, and sometimes qualitative, difference in their

response to orthostasis when compared with younger persons. There is generally a smaller reflex increase in heart rate (HR) (Dambrink & Wieling, 1987; Ebert, Hughes, Tristani, Barney, & Smith, 1982; Frey & Hoffler, 1988) most likely due to a decreased HR responsiveness in the high-pressure baroreflex system (Gribbin et al., 1971). Mean arterial pressure (MAP) may therefore be maintained with less of a reliance on HR (Jansen et al., 1989) and more of a reliance on increases in peripheral vascular resistance and diastolic blood pressure (DBP) (Ebert et al., 1982; Frey & Hoffler, 1988). In addition, while younger persons usually demonstrate an increase or no change in systolic blood pressure (SBP) when moving from sitting to standing (Convertino et al., 1984; Dambrink & Wieling, 1987), older persons often see a decrease (Dambrink & Wieling, 1987). This may be due to arterial rigidity, which decreases the ability of the vasculature to adjust to changes in pressure (Jansen et al., 1989; Smith and Fasler, 1983), or to baroreflex impairment (Lipsitz, 1989).

Whether the responses to an orthostatic stress can be improved after endurance training in the elderly is not known. Some of the components involved in the reflex responses to orthostasis may be irreversibly altered in the elderly (e.g., aortic distensibility, β -adrenergic sensitivity, cardiac and vascular compliance). Another problematic issue is that some of the changes produced by the aging process are in the same direction as those produced in younger persons who “improve” their responses to orthostasis after training. For example, an improved response to head-up tilt after training in young persons generally involves a decrease in HR and rate-pressure product associated with an increase in plasma volume (PV) (Convertino et al., 1984; Shvartz et al., 1981). In the elderly, the HR and SBP responses to tilt are already attenuated (Gribbin et al., 1971) and an improved response to tilt after

training may therefore involve increases, rather than decreases, in HR or SBP.

An understanding of the responses of elderly persons to an orthostatic stress after training first involves an investigation of how resting parameters may be altered with training and how training interacts with aging to produce changes. The response to an orthostatic stress before and after a period of training must also be described, taking into account both training and possible aging effects.

Responses to Endurance Training

Resting Heart Rate (HR), Stroke Volume (SV), and Cardiac Output (\dot{Q})

The decline in resting HR after endurance training is well documented in young and middle-aged persons. The magnitude of the decrease ranges from 4 to 8 beats \cdot min⁻¹ (Convertino et al., 1980a; Convertino et al., 1983; Convertino et al., 1984; Convertino et al., 1991; Greenleaf, Sciaraffa, Shvartz, Keil, & Brock, 1981; Hartley et al., 1969; Oscai et al., 1968; Pollock et al., 1976; Pollock et al., 1971; Seals & Chase, 1989) and may be related to training-induced hypervolemia (Fortney, Wenger, Bove, & Nadel, 1983). Other factors related to this decrease include decreased sympathetic nervous system (SNS) activity (Bjorntorp, 1987; Katona, McLean, Dighton, & Guz, 1982) and/or increased in parasympathetic tone (Barney, Ebert, Groban, & Smith, 1985; Kenney, 1985; Seals & Chase, 1989). Declines in resting HR may be independent of the body position in which the HR is measured. Greenleaf et al. (1981) found nearly equal decreases in resting HR in the supine and sitting positions after 8 days of cycle ergometry training (8 and 7 beats \cdot min⁻¹, respectively).

Some authors claim that a resting bradycardia does not occur with training in the elderly (Lampman & Savage, 1988). However, this conclusion is based partially on the results from studies on institutionalized subjects (Clark, Wade, Massey, & Van Dyke, 1975; Stamford, 1972) or on programs using "light" exercise (Emes, 1979). Nevertheless, even some studies using a moderate exercise intensity (Barry, Daly, Pruett, Steinmetz, Page, Birkhead, & Rodahl, 1966; Meredith et al., 1989; Schocken, Blumenthal, Port, Hindle, & Coleman, 1983) have failed to document significant decreases in resting HR. This is in contrast to other studies showing declines in resting HR in the elderly after training to be of approximately the same magnitude as documented in younger subjects. Braith et al. (1990) found a small ($3 \text{ beats} \cdot \text{min}^{-1}$) but significant decrease in HR after 3 months of endurance training at 50-70% HRR_{max} in healthy 60 to 79 year olds. A similar small decrease was noted by Adams and deVries (1973) in elderly women after 3 months of training at a minimum of 60% $\dot{V}\text{O}_2\text{max}$. Cononie et al. (1991) found a slightly greater decline ($5 \text{ beats} \cdot \text{min}^{-1}$) in healthy 70-79 year olds after six months of endurance training at 75-85% $\dot{V}\text{O}_2\text{max}$. Older hypertensives may have even larger reductions in HR as a result of training (e.g., 8-13 beats; Hagberg et al., 1989b).

Stroke volume at rest has been shown to be unchanged (Ekblom, Astrand, Saltin, Stenberg, & Wallstrom, 1968) or increased (Convertino et al., 1991; Hartley et al., 1969) after strenuous physical training in young and middle-aged persons. Increases may be related to training-induced hypervolemia and elevated central venous pressure (CVP) (Convertino et al., 1991), or to changes in such cardiac loading conditions as decreased peripheral resistance and increased left ventricular EDV (Ehsani, 1987). In instances where SV was increased, resting \dot{Q} remained the same despite an increased

BV, due to the reduction in resting HR (Convertino et al., 1991; Hartley et al., 1969).

The data on changes in resting SV or \dot{Q} with training in the elderly are scarce. In one of the few reported studies, Hagberg et al. (1989b) found that elderly hypertensives did not increase their resting SV or their blood or plasma volumes after 9 months of low- or moderate-intensity exercise training. However, the low-intensity exercise group had a reduction in resting \dot{Q} , while the moderate-intensity group had a reduction in total peripheral resistance. No potential mechanisms were proposed to explain the different responses. Similarly, Schocken et al. (1983) reported that neither resting \dot{Q} nor resting SV changed after training in the elderly. They also found that contractile function, as measured by an increase in left ventricular (LV) ejection fraction and LV ESV, did not change with training.

Blood Pressure (BP)

Since the level of mean BP is the product of flow ($\dot{Q} = \text{HR} \times \text{SV}$) and peripheral resistance, changes in one or both of these factors as a result of exercise training could effect BP changes. If SV remains unchanged, reductions in HR and \dot{Q} will provide a blood pressure-lowering effect. Reductions in peripheral resistance may also act to lower BP.

Mechanisms associated with these changes include a decrease in SNS activity, resetting and/or increased sensitivity of baroreceptors, altered distribution of BV, altered pressure-natriuresis function, alterations in the renin-angiotensin axis, altered sensitivity of vascular α - and β -receptors, and alterations in the release or actions of endothelium-derived vasorelaxants and vasoconstrictors (Kenney & Zambraski, 1984; Tipton, 1991). It has also been hypothesized that physical activity sends specific afferent signals to the

central nervous system that stimulate central endorphin production and cause a decrease in resting HR and \dot{Q} through central inhibition of SNS activity (Bjorntorp, 1987). In addition, since insulin is stimulated by β -adrenergic activity, lowered SNS activity may also result in a decrease in plasma insulin concentration. This may help to decrease BP by decreasing sodium (Na^+) reabsorption in the kidney (Bjorntorp, 1987; Kenney & Zambraski, 1984). Greenleaf et al. (1981) hypothesize that the drop in diastolic BP after training is a result of the continued stimulation of both vasopressin and the renin-angiotensin system during exercise, resulting in a diminished vasoconstrictive response for some time after exercise; i.e., "fatigue" of the vasoconstrictor response. Confounding factors include a concomitant weight loss with training, which independently decreases catecholamine release and BP (Tipton, 1991).

According to several recent reviews, endurance training in young and middle-aged persons with mild essential hypertension can lower both SBP and DBP 8-10 mmHg (Bjorntorp, 1987; Hagberg, 1990; Hagberg & Seals, 1987). Training in older (> 60 years) hypertensives (Hagberg et al., 1989b) and normotensives (Braith et al., 1990; deVries, 1970; Emes, 1979; Stamford, 1972) can have the same effect. Despite the reductions seen in some normotensives, it is commonly thought that the BP-lowering benefits to be derived from endurance training are dependent on the initial BP level: persons with normal initial BP often do not see reductions with training (Adams & deVries, 1973; Kilbom et al., 1969; Pollock et al., 1976; Schocken et al., 1983) while those with mild to moderate elevations in BP (>140/90 mmHg) are likely to see improvements with training (Kiyonaga et al., 1985). This phenomenon has been documented by Cononie and coworkers (1991) in a study on healthy 70-79 year olds. After six months of endurance training at

75-85% $\dot{V}O_{2\max}$, there were decreases in SBP, DBP, and mean arterial blood pressure (MAP) of 4, 5, and 4 mmHg, respectively. However, when subjects with initial blood pressures of >140/90 mmHg were analyzed separately, the decreases were 8, 9, and 8 mmHg for SBP, DBP, and MAP, respectively.

Maximal Aerobic Power

Endurance training programs of 6 to 12 months duration that meet the American College of Sports Medicine's (ACSM) criteria for developing and maintaining cardiorespiratory fitness (ACSM, 1990) generally result in improvements in $\dot{V}O_{2\max}$ ranging from 15-30%. The magnitude of improvement is dependent on the frequency, intensity and duration of training (Atomi, Ito, Iwasaki, & Miyashita, 1978; Gettman et al., 1976; Miles et al., 1976).

Although there is a decrease in maximal aerobic power with age (Buskirk & Hodgson, 1987), the relative training-induced improvement in $\dot{V}O_{2\max}$ that can be made by healthy elderly individuals is similar to that seen in younger individuals (Cress et al., 1991; Hagberg et al., 1989a; Meredith et al., 1989; Seals et al., 1984; Sidney & Shephard, 1978) when training programs are designed according to the ACSM (1990) recommendations. For example, training for more than two days per week at either 60 or 80% maximal HR reserve (HRR_{\max}), resulted in improvements in $\dot{V}O_{2\max}$ of 14 and 29%, respectively, in elderly persons (Sidney & Shephard, 1978). Similarly, training 3 days per week for six months at 75-85% HRR_{\max} resulted in a 20% improvement in $\dot{V}O_{2\max}$ in elderly men and women (Hagberg et al., 1989a).

It appears that improvements in $\dot{V}O_{2\max}$ in the elderly are due primarily to peripheral, as opposed to central, adaptations. While both

central (i.e., increased maximal SV, maximal \dot{Q} , and maximal myocardial oxygen $[O_2]$ consumption) and peripheral (increased maximal arteriovenous O_2 difference) adaptations have resulted from endurance training in young and middle-aged men (Ekblom et al., 1968; Hartley et al., 1969) and in cardiac patients (Ehsani, Heath, Martin, Hagberg, & Holloszy, 1984; Ehsani, Martin, Heath, & Coyle, 1982), the evidence for improved central parameters after training in elderly individuals is sparse and inconclusive (Ehsani, 1987). Indirect evidence for central adaptations is provided by Heath, Hagberg, Ehsani, and Holloszy (1981) who found that values for maximal O_2 pulse were similar for young and master athletes, and both were higher than for a group of sedentary middle-aged individuals. This suggested that the higher $\dot{V}O_{2\max}$ in the master athletes compared with the sedentary subjects could have been mediated through a higher maximal SV, since maximal HR was similar between the two groups. However, a higher maximal arteriovenous O_2 difference cannot be ruled out. Schocken and coworkers (1983) also provide evidence for an increase in maximal SV in the elderly. They found that although moderate- to high-intensity training (70-85% HR_{\max}) did not change resting SV, ESV, or EDV in elderly subjects, the calculated maximal exercise SV increased approximately 13 ml as a result of an increase in maximal LV EDV. Maximal \dot{Q} increased from 9.94 to 11.40 $L \cdot min^{-1}$, but this was not statistically significant.

Meredith and coworkers (1989) provided evidence for the peripheral adaptation hypothesis. After 12 weeks of cycle ergometer training at 70% HRR_{\max} , they found that elderly subjects demonstrated significant increases of 27 and 118% in muscle glycogen content and muscle oxidative capacity at rest, while younger subjects showed nonsignificant increases of 14 and 28%, respectively. However, part of the disparity in the results may be because both

young and old subjects made nearly identical absolute increases in $\dot{V}O_{2\max}$ (5.5 and 5.3 ml•kg⁻¹•min⁻¹, respectively). In relative terms, the elderly subjects increased $\dot{V}O_{2\max}$ 19.9%, compared with 12.1% for the young subjects.

Seals et al. (1984) also found evidence for peripheral, but not central, training adaptations in the elderly. They found that after 6 months of low-intensity training followed by 6 months of high-intensity training, 61-67 year-old men and women increased $\dot{V}O_{2\max}$ approximately 30%. Since maximal \dot{Q} was not significantly increased, the increase in $\dot{V}O_{2\max}$ appeared to be mediated primarily through a 14% increase in the maximal arteriovenous O₂ difference.

Increase in Strength and Muscle Mass

Changes in body composition as a result of endurance training are commonly assessed using hydrostatic weighing or skinfolds. Using these methods, lean body mass changes either not at all (Hagberg et al., 1989a; Kilbom et al., 1969) or increases a small amount (Boileau, Buskirk, Horstman, Mendez, & Nicholas, 1971; Wilmore et al., 1980) as a result of endurance training. Using urinary creatinine as a measure of muscle mass, Meredith et al. (1989) also found no increase in muscle mass after 12 weeks of endurance training at 70% $\dot{V}O_{2\max}$ in the elderly.

Due to the specific nature of training adaptations, it would not be expected that strength would substantially increase as a result of endurance training. Consequently, very few endurance training studies have incorporated or reported strength testing measures. An early study (Barry, Steinmetz, Page, & Rodahl, 1966) found no increase in knee extension or elbow flexion strength after 3 months of cycle ergometer training in the

elderly. In a more recent study, however (Graves et al., unpublished), there was a strong trend toward an increase in leg strength in endurance trained 70-79 year olds, many of whom used uphill treadmill walking as a mode of training.

Responses to Strength Training

Although the response to strength training varies widely among individuals and studies, the average improvement in strength for young and middle-aged men and women for most muscle groups appears to be approximately 25-30% (Fleck & Kraemer, 1987) and is often associated with an increase in fat free weight (FFW) (Hurley et al., 1984). Older individuals are capable of making comparable changes with appropriately designed programs (Aniansson & Gustafsson, 1981; Aniansson, Ljungberg, Rundgren, & Wetterqvist, 1984; Chapman, deVries, & Swezey, 1972; Liemohn, 1975; Moritani & deVries, 1980). In some studies using elderly individuals, however, moderate- to high- intensity resistance training has resulted in greater increases in strength (e.g., 50-230%) (Fiatarone et al., 1990; Frontera et al., 1988; Kauffman, 1985; Perkins & Kaiser, 1961). This may be due to the lower initial level of strength and thus the greater relative potential for strength development.

Changes in muscle morphology that occur with aging include a decrease in the total number of both Type I and Type II fibers, with a greater proportional loss of the Type II fibers (Evans, 1986; Larsson, Sjodin, & Karlsson, 1978; Larsson, Grimby, & Karlsson, 1979). This age-related atrophy is thought to be caused by either a reduction in physical activity (Aniansson & Gustafson, 1981; Larsson et al., 1978) or a reduced capacity to repair or replace damaged muscle cells (Evans, 1986).

Although aging-related changes in muscle morphology can be partially reversed as a result of resistance training, the reported changes vary among studies. This may be due to differences in training intensity, muscle groups trained or tested, or even possibly to gender-specific adaptations. Cress et al. (1991) found an increase in the Type IIb fiber cross-sectional area, with maintenance of the Type I and IIa fiber cross-sectional area, after 50 weeks of low to moderate aerobic/resistance training in septuagenarian women. Both Aniansson and Gustafsson (1981) and Aniansson et al. (1984) noted an increase in the percentage, but not in the cross-sectional area, of Type IIa fibers after resistance training in elderly men and women. On the other hand, Larsson (1982) found that the cross-sectional area of both Type I and Type II fibers increased 31.8 and 51.5%, respectively, with 15 weeks of knee extensor training in 56-65 year old men. Frontera et al. (1988) also found significant increases of 33.5 and 27.6% in Type I and II fiber cross-sectional area after 12 weeks of strength training in 60-72 year old men.

Hormonal, and Blood/Plasma Volume Responses to Training: Resting Values

Blood/Plasma Volume

While some early studies reported no change in BV as a result of training (Bass, Buskirk, Iampietro, & Mager, 1958; Dill, Hall, Hall, Dawson, & Newton, 1966), most recent studies show that endurance training increases BV (Convertino et al., 1980a; Convertino, Greenleaf, & Bernauer, 1980; Convertino et al., 1983; Convertino et al., 1984; Convertino et al., 1991; Oscai et al., 1968). Associated with the increase in the plasma fraction of the blood and the constant red cell volume, there is a decrease in the hematocrit (Hct) and

the hemoglobin (Hb) concentration but a constancy in the Hb content (Convertino et al., 1980a; Oscai et al., 1968).

The training parameters of intensity, frequency and duration have all been hypothesized to affect BV increases. Two studies by Convertino and colleagues illustrate the possible effect of training intensity on BV expansion (Convertino et al., 1980a; Convertino et al., 1977). Both studies utilized an 8-day training protocol involving 2 hours of cycle ergometer exercise per day; intensity for the former study was 65% of $\dot{V}O_{2\max}$ while it was 50% of $\dot{V}O_{2\max}$ for the latter study. The regimen with the higher intensity produced an 18.7% (72 ml) higher increase in BV.

Intensity, however, cannot be the only factor influencing the magnitude of PV expansion. In two studies by Convertino and colleagues (Convertino et al., 1980a; Convertino et al., 1983), identical 8-day cycle ergometer training protocols at an intensity of 65% of $\dot{V}O_{2\max}$ for 2 hours per day induced 12.1 and 12.3% increases, respectively, in PV. However, a different investigative group (Greenleaf et al., 1981) found a similar (12.2%) increase in PV after a comparable training protocol at an exercise intensity of only 44% of $\dot{V}O_{2\max}$. It might be hypothesized that the potential for PV expansion is greater when the initial volume is lower since the relative volume expansions in these studies were similar, but the absolute increases were smaller in the Greenleaf et al. (1981) (385 ml vs. 427 ml in both Convertino et al. studies), indicating a smaller initial PV. On the other hand, Convertino et al. (1980a) compared the fitness level and relative hypervolemia of the subjects in their study with those of Oscai et al. (1968). The subjects in the Convertino et al. investigation had a higher initial fitness level ($57 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ vs. approximately $38.5 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) and a higher

initial PV (3500 ml vs. 3196 ml), yet they were able to achieve a greater relative PV expansion (12.1% vs 6.4%; 427 ml vs. 204 ml).

Frequency and duration of training are thought to affect training-induced hypervolemia. It has been speculated that regimens with consecutive days of training and/or exercise durations of two hours or more per day produce a greater hypervolemia than those which allow 1-2 days recovery between training sessions and/or use shorter exercise sessions (Convertino et al., 1980a). If program duration is held constant, particularly with shorter (e.g., 8 days) programs, this may hold true. An equally important factor in BV expansion, however, may be the total amount of work performed during the entire program. For example, Convertino et al. (1991) produced a 13% increase in PV with a 10-week training regimen where subjects exercised for 4 days per week, 30 minutes per day at 75-80% of $\dot{V}O_2\text{max}$. In the Convertino et al. (1980a) study, a 12.1% increase in PV was achieved with an 8-day protocol, where subjects exercised for 2 hours per day at 65% of $\dot{V}O_2\text{max}$. It is possible that the lower training frequency and shorter duration in the former study was offset by the higher intensity and longer program duration to produce an equivalent PV expansion.

In contrast, Oscai et al. (1968) produced only a 6.4% increase in PV with training for 30 minutes per day, 3 days per week for 16 weeks. Although the training intensity relative to $\dot{V}O_2\text{max}$ was not specified, the training HR data suggest an intensity similar to that used in the Convertino et al. (1991) study. Clearly, there are other factors or combinations of factors influencing the degree to which PV can be expanded due to a training regimen.

Hormonal factors associated with training-induced hypervolemia appear to be the stimulation of vasopressin (AVP) and renin (PRA) production during exercise (approximately five- to ninefold increases), which

facilitate retention of Na^+ and water; and an increase in plasma albumin content, which provides an increased water-binding capacity for the blood (Convertino et al., 1980a; Convertino, Keil, Bernauer, & Greenleaf, 1981). This conclusion is supported by data from Greenleaf et al. (1981) who found that subjects exercising in the heat had greater increases in AVP and PRA during exercise and a larger PV after training than subjects exercising in a more moderate temperature. Resting values of AVP and PRA, however, were unchanged with training (Convertino et al., 1980a; Convertino et al., 1983; Greenleaf et al., 1981; Convertino et al., 1991).

Few studies have documented the PV responses to training in older individuals. Resting PV does not appear to change with age up to age 40 (Chien, Usami, Simmons, McAllister, & Gregersen, 1966) but cross-sectional and longitudinal data with older individuals are lacking. Convertino et al. (1980a) hypothesized that training-induced hypervolemia might be less in older individuals due to a decreased physical working capacity. However, since training intensity expressed as a percentage of $\dot{V}\text{O}_2\text{max}$ appears to be a potent stimulus for PV expansion, the relative hypervolemia induced by training in older individuals may be equal to that of younger individuals training at the same relative intensity. Indirect evidence for the Convertino et al. hypothesis is offered by the data of Kilbom et al. (1969). In this study, 38-55 year old men increased $\dot{V}\text{O}_2\text{max}$ by 14% after 2 months of endurance training; however, there were no changes in resting Hb and Hct. Although PV was not measured, the data suggest that it did not change since an increase in PV is usually accompanied by decreases in Hb and Hct (Convertino et al., 1980a; Oscai et al., 1968). An aging effect (a decrease in aldosterone secretion, and a decrease in plasma concentration and renal sensitivity to vasopressin [anti-diuretic hormone]), and not the decline in physical working capacity,

would more likely contribute to a lack of change in PV in older persons (Greggerman & Bierman, 1981; McGinty et al., 1988).

Vasoactive Hormones

Vasopressin (AVP). The most potent stimulus for AVP secretion is an increase in blood osmolality sensed by osmoreceptors in or near the hypothalamus. Increases as small as 1-2% above $280 \text{ mOsm} \cdot \text{L}^{-1}$ are sufficient to elicit AVP secretion. A secondary influence on AVP secretion is a BV change sensed by both high- and low-pressure mechanoreceptors. The high-pressure baroreceptors in the carotid sinus and aortic arch are sensitive to changes in arterial pressure while low-pressure (cardiopulmonary) baroreceptors, located in the atria, the pulmonary veins, and within the walls of the heart, respond to changes in intracardiac pressures. Reductions in arterial, central venous, or atrial pressure, such as would be induced by head-up tilt, decrease afferent nerve activity and release inhibitory activity in the cardiovascular centers of the central nervous system. A series of reflexes ensue which act to maintain arterial pressure by increasing \dot{Q} and/or peripheral resistance. The end result is an increase in HR and contractility, increased veno- and vasoconstriction, and reduced blood flow to the skin, skeletal muscles, kidney and splanchnic area (Convertino, 1987; Guyton, 1991; Goodman & Frey, 1988). An increase in vasoactive hormone (AVP, norepinephrine, and renin-induced angiotensin II [AII]) release is an integral part of this response. Conversely, increases in central venous or atrial pressure induced by supine posture or water immersion would produce opposite changes. Supine resting values of AVP average $2.7 \pm 1.4 \text{ pg} \cdot \text{ml}^{-1}$ (Labhart, 1986).

Training-induced increases in BV cause parallel increases in CVP (Convertino et al., 1991) and are of the magnitude (10-15%; Convertino et al., 1980a; Convertino et al., 1983; Convertino et al., 1991; Greenleaf et al., 1981) where AVP would be expected to decrease. Cross-sectional studies have found that acute volume expansion or water immersion stimulate the suppression of AVP and secretion of atrial natriuretic factor both in animals (Johnson, Zehr, & Moore, 1970) and humans (Gauer & Henry, 1963; Norsk, Bonde-Petersen, & Warberg, 1985; Thompson, Tatro, Ludwig, & Convertino, 1990; Volpe et al., 1989). Conversely, Harrison et al. (1986) found that acute changes in central BV induced by dehydration and orthostasis induced increases in AVP. In contrast, Norsk, Bonde-Petersen, & Warberg (1986) did not find a relation between acute CVP changes, induced by lower body negative pressure (LBNP) or lower body positive pressure, and AVP secretion, and concluded that the cardiopulmonary mechanoreceptors did not strongly influence AVP secretion.

Although studies using acute volume changes to stimulate or suppress AVP provide evidence that cardiopulmonary receptors play a role in AVP secretion, they do not adequately address the issue of the effect of chronic changes in volume and CVP on hormonal secretion. It has been hypothesized that endurance training causes a resetting and/or a decrease in the sensitivity of the cardiopulmonary receptors (Convertino, 1987). This results in unchanged basal levels associated with increased BV, together with either a reduced suppression of AVP when CVP is increased (e.g., during water immersion or lower body positive pressure), or a reduced secretion of AVP when CVP is reduced (e.g., during tilt or LBNP). A resetting of the stimulus-response relation between BV, CVP, and AVP secretion is suggested by the data of Freund et al. (1988) who found that endurance-trained

individuals have resting levels of AVP similar to those of sedentary individuals. A decrease in sensitivity of the cardiopulmonary receptors is suggested by studies which have found that endurance-trained individuals exhibited a lesser diuretic response (i.e., a reduced suppression of AVP) in response to water immersion (Boning & Skipka, 1979; Claybaugh et al., 1986; Skipka, Boning, Deck, Kulpmann, & Meurer, 1979) or water intake (Claybaugh et al., 1986; Freund et al., 1988) as evidenced by a lower urine flow.

Longitudinal studies provide the best insight into the response of resting AVP levels to physical training and into possible alterations in cardiopulmonary baroreceptor sensitivity. Convertino et al. (1980a) and Convertino et al. (1983; 1991) found that resting AVP did not change after training programs that increased $\dot{V}O_{2\max}$ by 8-20%. In their most recent investigation, Convertino et al. (1991) measured BV, CVP, and resting hormonal levels. They found that training resulted in parallel increases in BV and CVP, but without any increase in MAP or vascular compliance. In addition, there were no changes in resting levels of AVP, ALDO, or atrial natriuretic factor suggesting that the chronic increase in CVP caused a resetting of the cardiopulmonary stimulus-response mechanism.

Renin. Renin is synthesized and secreted into the blood by the juxtaglomerular (JG) cells in the afferent arterioles of the glomeruli. Juxtaglomerular cells secrete renin in response to decreased pressure in the afferent arterioles as well as in response to sympathetic stimulation, decreased Na^+ load in the tubular fluid, or a drop in atrial pressure (Goodman & Frey, 1988; Kiowski & Julius, 1978). All of these stimuli are related to a decrease in BV and/or a drop in arterial pressure. Normal supine resting values for renin activity in normotensive individuals range from 1-2 ng Angiotensin

$\text{l} \cdot \text{ml}^{-1} \cdot \text{h}^{-1}$ (Labhart, 1986), but may be lower in the elderly (Cleroux et al., 1989; Greggerman & Bierman, 1981).

Although it might be expected that training-induced increases in BV (Convertino et al., 1980a; Convertino et al., 1980b; Convertino et al., 1983; Convertino et al., 1991; Oscai et al., 1968) or decreases in SNS activity (Bjorntorp, 1987; Katona et al., 1982) would reduce renin secretion as it does in acute volume changes (Thompson et al., 1990), the increase in volume is not associated with increases in mean arterial pressure (Convertino et al., 1991) or with changes in plasma Na^+ concentrations (Convertino et al., 1980a; Freund et al., 1988). Accordingly, most studies find that renin activity in younger individuals does not change with training. Both Convertino et al. (1980a) and Convertino et al. (1983) found unchanged resting levels after an exercise protocol (8 days of cycle ergometry for 2 hours per day at 65% $\dot{V}\text{O}_{2\text{max}}$) that induced 12.1-12.3% increases in PV. Wade et al. (1981) also found resting levels to be unchanged in endurance runners during and after 20 days of running an average of 28 km per day.

The data from cross-sectional studies largely support this conclusion. Both Freund et al. (1988) and Skipka et al. (1979) found no difference in resting PRA levels between trained and untrained individuals. However, one study (Fagard et al., 1985) found lower resting PRA values in endurance-trained athletes.

The data regarding changes in resting levels of renin after training in the elderly are sparse and contradictory. Braith et al. (1990) found decreases in resting PRA associated with decreases in resting BP in healthy 60 to 79 year olds after 3 months of exercise training at 50-70% HRR_{max} . On the other hand, Hagberg et al. (1989b) found that after 9 months of exercise training in elderly hypertensives, there were equivalent reductions in resting PRA for

both exercising and control groups. This did not appear to be associated with the BP changes, however: subjects exercising at low (50% $\dot{V}O_{2\max}$) intensity experienced significantly greater reductions in BP than the control or moderate-intensity (70-85% $\dot{V}O_{2\max}$) exercise groups, but with equivalent reductions in PRA.

Catecholamines. Norepinephrine (NE) levels are generally considered representative of sympathetic tone (Mazzeo, 1991), although this conclusion has been challenged (Floras et al., 1986). The possibility that plasma NE concentrations may not represent sympathetic activity after training because of down regulation of adrenergic receptors has not been investigated (Tipton, 1991). Resting plasma levels of NE average 66-390 pg•ml⁻¹ while resting EPI levels average 10-70 pg•ml⁻¹ (Cryer, 1980). Resting levels of NE are increased with age, while EPI concentrations remain unchanged (Gregerman & Bierman, 1981; Lipsitz, 1989).

Training is associated with a decrease in SNS activity as evidenced by a decrease in plasma NE concentration, particularly in hypertensives (Hagberg et al., 1989b; Kiyonaga et al., 1985; Tipton, 1991). However, Convertino et al. (1991) found no change in resting levels of NE after 10 weeks of training in young normotensive men. Changes in body weight associated with training may independently result in decreases in catecholamine release, rendering conclusions about the effect of training alone difficult (Tipton, 1991). The reduction in resting NE is thought to result in a decrease in BP through decreases in resting HR and \dot{Q} . However, the data regarding the response of peripheral resistance are inconsistent: some investigators have found that the decrease in NE is associated with a decrease in peripheral resistance while others have found either an increase or no change (Tipton, 1991).

Data on post-training resting catecholamine concentrations in the elderly are scarce. Hagberg et al. (1989b) found that 9 months of exercise training in elderly hypertensives did not reduce supine or standing NE levels compared with initial within-group levels. However, because of an increase in NE in the control group, the changes from pre- to post-training in the exercise groups were significant. Epinephrine (EPI) levels (both supine and standing) did not change with training in either exercise group.

Summary. Based on results from studies inducing acute central BV changes, increases in BV should produce increased stimulation of the cardiopulmonary baroreceptors and induce a suppression of AVP and renin. The bulk of the data, both cross-sectionally and longitudinally, suggest that this does not occur when central BV is increased chronically. This supports the hypothesis (Convertino et al., 1991) that the continual stimulation of the cardiopulmonary receptors produces an attenuation of the stimulus-response mechanism or a resetting of the receptors to operate at a higher CVP.

Norepinephrine levels, however, are more commonly seen to decrease with training. These reduced levels are associated with decreases in BP or peripheral resistance. Training-induced losses in body weight may independently reduce catecholamine levels.

Hormones Associated with Fluid Volume Control: Aldosterone (ALDO)

The plasma concentration of AII is the most potent stimulus for ALDO secretion; increased adrenocorticotrophic hormone (ACTH) and potassium (K^+) concentrations are also potent stimuli. Since the rate-limiting step in the production of AII is the cleavage by renin of angiotensinogen to angiotensin I (AI), the secretion of renin by the kidney is a major regulator of ALDO secretion. Therefore, the forces that stimulate renin secretion will ultimately

increase ALDO secretion. Increased ALDO causes an increase in the reabsorption of Na^+ in the renal collecting ducts along with an obligatory retention of water, and an increase in the excretion of K^+ . Normal resting values for supine subjects range from 20-100 $\text{pg} \cdot \text{ml}^{-1}$ (Labhart, 1986). Resting levels in the elderly are approximately 40% lower (Gregerman & Bierman, 1981).

Most studies show that training does not affect resting ALDO levels. This is not surprising in light of the constancy of resting renin activity levels previously cited. Convertino and coworkers (1991) found no changes in resting ALDO levels after a 10 week (4 days per week at 75-80% of $\dot{V}\text{O}_2\text{max}$) training regimen. Cross-sectional studies (Freund et al., 1988; Wade et al., 1981) also have found no differences in resting ALDO levels between trained and untrained individuals. One study, however, did find that trained subjects had lower resting levels of ALDO compared with untrained subjects, but that this difference did not correspond to the resting renin activity levels (Skipka et al., 1979).

Data on training changes in resting ALDO concentrations in the elderly are scarce. Braith et al. (1990) found that 3 months of exercise training in 60 to 79 year-olds did not alter resting ALDO levels, despite evidence for a decrease in both resting potassium (K^+) and resting renin activity.

Adrenocorticotrophic Hormone (ACTH)

Adrenocorticotrophic hormone causes the adrenal cortex to secrete cortisol and ALDO. However, ACTH is not as important a regulator of ALDO secretion as is AII, but it is required for optimal secretion (Goodman, 1988; Guyton, 1991). An important factor in the measurement of resting ACTH levels is the time of day of measurement: ACTH demonstrates a circadian

rhythm, with highest levels in the early morning. Morning values for the healthy adult range from 10-100 pg•ml⁻¹, while evening values range from 5-20 pg•ml⁻¹ (Labhart, 1986). Aging does not appear to change resting ACTH levels (Everitt, 1980; Gregerman & Bierman, 1981).

The response of resting ACTH levels to training is not known. However, since acute distension of the right atrium inhibits ACTH release (Cryer & Gann, 1974), it might be hypothesized that the increase in BV that accompanies training would reduce basal ACTH secretion. On the other hand, if there is a resetting and/or a reduction in sensitivity of the atrial receptors mediating ACTH release as there appears to be for AVP and renin release, basal levels would not be affected.

Protein (PROT), Sodium (Na⁺) and Potassium (K⁺)

The normal resting value for PROT in the plasma is 1.2 mOsm•L⁻¹, or 7.3 gm•dl⁻¹, while the normal resting values for Na⁺ and K⁺ are 143 and 4.2 mOsm•L⁻¹, respectively (Guyton, 1991). Protein and K⁺ together provide only about 2% of the total plasma osmolar activity while Na⁺ is responsible for approximately 51% of the total osmolar activity. Changes in plasma Na⁺ concentrations affect osmoreceptors in or near the anterior hypothalamus, which in turn control AVP secretion by the posterior pituitary gland.

Plasma proteins are responsible for producing capillary osmotic pressure since they do not readily diffuse through the capillary membrane. Although, from a homeostatic point of view, it would not be expected that the concentrations of PROT, Na⁺, or K⁺ would change with training, the training-induced increase in BV would require that the total PROT and osmolar content increase in parallel in order to retain the added fluid and maintain homeostasis. In addition, because the osmolality-AVP feedback

system is sensitive to small changes in osmolality, and because resting levels of AVP appear to be unchanged with training (Convertino et al., 1980a; Convertino et al., 1983; Convertino et al., 1991), it would be expected that resting plasma levels of Na^+ would be unaltered with exercise training. Indeed, Convertino et al. (1980a) found that an 8.1% (457 ml) increase in BV was accompanied by an increase in total osmolar and PROT content, but not concentration.

This conclusion is supported by the cross-sectional data of Freund et al. (1988) who noted similar plasma Na^+ , K^+ , and PROT concentrations in trained and untrained subjects. One study, however, noted a lower resting PROT concentration in trained subjects ($6.35 \text{ g} \cdot \text{dl}^{-1}$) compared with their untrained counterparts ($6.9 \text{ g} \cdot \text{dl}^{-1}$) (Boning & Skipka, 1979).

There has also been a report of decrease in plasma K^+ from 4.2 to 3.7 $\text{mEq} \cdot \text{L}^{-1}$ as a result of 4 months of intensive training (Rose, 1975). This may be due to the post-exercise increase in ALDO that occurs in response to transient episodes of hyperkalemia during exercise, and which results in a "rebound" hypokalemia. Cross-sectional data (Claybaugh et al., 1986; Wade et al., 1981) showing an increased ALDO response in trained individuals to water immersion and daily long-distance running lend indirect support to this theory. However, the finding of greater ALDO responsiveness in trained individuals is not universal (Freund et al., 1988; Skipka et al., 1979).

An alternative explanation for the resting hypokalemia seen after training involves an increase in resting muscle membrane potential, favoring a movement of K^+ into the muscle cells. Six weeks of treadmill training in dogs increased the muscle membrane potential from -91 to -103 mV. Hyperpolarization has also been seen in humans trained for long-distance running and correlates linearly with the $\dot{V}\text{O}_2\text{max}$ (Knochel, 1985).

Data on the response of resting K^+ , Na^+ , and PROT levels after training in elderly individuals are sparse. Braith et al. (1990) found a decrease in resting K^+ from 4.24 to 3.94 mEq•L⁻¹, but an unchanged resting ALDO, in elderly subjects after 3 months of endurance training; no mechanisms were proposed to explain the result.

Cardiovascular, Hormonal, and Plasma Volume Responses to Tilt: Pre- and Post-training

Head-up tilt is a method used to study the reflex mechanisms associated with the response to orthostasis. Because muscular activity in the legs can be minimized, as compared with passive standing, the contribution of cardiovascular reflexes to the maintenance of arterial pressure can be better distinguished. As a response to the venous pooling induced by upright tilt, CVP, EDV, SV, and \dot{Q} are sequentially reduced. There is also a gradual decrease in blood flow in the kidney, and in the resting arm and leg muscles (Convertino, 1987).

If \dot{Q} is decreased without an increase in peripheral resistance, arterial pressure and cerebral perfusion will fall, and syncope will ensue. The ability of the body to resist the fall in arterial pressure is dependent on the responsiveness and interaction high- and low-pressure baroreceptor systems, myocardial function, arterial and venous tone, and neuroendocrine secretions.

The cardiovascular and hormonal responses to tilt cannot be directly compared among different investigations due to the widely differing protocols. Differences exist in the length of the pre-tilt control period, the angle and duration of tilt, use of a saddle or footplate, and the timing of measurements. The angle of tilt may be a particularly important parameter

(Fitzpatrick, Theodorakis, Vardas, & Sutton, 1991): for example, a 45° tilt represents approximately 70% of the stresses imposed by upright posture (Jansen et al., 1989) while a 70° head-up tilt is nearly equivalent to the stress of upright posture (Lye, Vargas, Faragher, Davies, & Goddard, 1990; Wieling et al., 1983). The magnitude of cardiovascular and hormonal responses would be expected to vary accordingly, as documented for the HR and thoracic BV responses by Smith et al. (1984). Nevertheless, it may be possible to deduce qualitative conclusions from earlier studies.

Heart Rate, Stroke Volume, Cardiac Output, and Blood Pressure

The increase in HR from supine to upright posture in young subjects is well documented and appears to vary based on the angle and duration of tilt. Increases of approximately 10 to 30 beats•min⁻¹ are generally reported (Beetham & Buskirk, 1958; Convertino et al., 1984; Davies, Slater, Forsling, & Payne, 1976; Greenleaf et al., 1981; Huber et al., 1988; Lee, Lindeman, Yiengst, & Shock, 1966; Matalon & Farhi, 1979; Matzen, Knigge, Schutten, Warberg, & Secher, 1990; Sannerstedt, Julius, & Conway, 1970; Shannon et al., 1991; Solomon, Atherton, Bobinski, & Green, 1986; Vargas et al., 1986; Wieling et al., 1983; Williams, Walsh, Lightman, & Sutton, 1988), although smaller increments have been seen (Dambrink & Wieling, 1987). Stroke volume decrements during tilt range from 30 to 50% (Banner et al., 1990; Blomqvist & Stone, 1983; Mangseth & Bernauer, 1980; Matalon & Farhi, 1979; Sannerstedt et al., 1970; Vargas et al., 1986). Despite compensatory increases in HR, \dot{Q} generally decreases approximately 20-30% (Banner et al., 1990; Blomqvist & Stone, 1983; Mangseth & Bernauer, 1980; Matalon & Farhi, 1979; Sannerstedt et al., 1970; Vargas et al., 1986), although both Lee et al. (1966) and Matzen et al. (1990) reported smaller decrements.

The changes with posture in older individuals are generally of a smaller magnitude. On an absolute basis, HR increments during tilt are less than in young persons, although at least one study found no difference in the response (Lipsitz, Mietus, Moody, & Goldberger, 1990). Increases of only 10-15 beats•min⁻¹ are common (Kenny et al., 1987; Lee et al., 1966; Lye et al., 1990; Shannon et al., 1991; Vargas et al., 1986). However, one investigation (Ecoffey, Edouard, Pruszczyński, Taly and Samii, 1985) found that HR did not increase in elderly men during 30° tilt. Although this may be due to the low angle of tilt used, another investigation (Dambrink and Wieling, 1987) also found small HR increments (0-5 beats•min⁻¹) in 60 to 90 year-olds during a 70° tilt.

Even on a relative basis, HR increments during tilt are smaller in older individuals. Jansen et al. (1989) reported that elderly normotensives had a 10-15% increases in HR compared with 20-25% increments in young normotensives. Several investigators (Dambrink & Wieling, 1987; Norris, Shock, & Yiengst, 1953; Smith, Barney, Groban, Stadnicka, & Ebert, 1985) have also found that the peak steady state HR response to orthostatic changes or to neck suction took longer to achieve in older individuals.

Stroke volume during tilt decreases approximately 25-40% in older individuals (Lee et al. 1966; Lye et al., 1990; Shannon et al., 1991; Vargas et al., 1986). Shannon et al. (1991) found that the greater reduction in SV in older, as compared with younger, individuals was related to their inability to decrease ESV despite similar reductions in EDV. It was hypothesized that the inability to decrease ESV was due to aging changes in the vascular system.

The data comparing postural changes in \dot{Q} in young and old subjects are contradictory. Vargas et al. (1986) found equivalent resting and tilt \dot{Q} values in both young (\bar{x} = 29.9 yrs) and old (\bar{x} = 70.4 yrs) subjects. On the other hand, Shannon et al. (1991) found similar resting \dot{Q} values in old and

young subjects, but found that young subjects increased \dot{Q} by 19% during a 60° tilt while old subjects experienced an 18% decrease. Finally, Lee et al. (1966) found that older subjects had a 12% fall in cardiac index while young subjects saw only a 3% drop.

A comparison of the BP responses of old and young subjects during tilt reveals a variety of response patterns. Most investigations have found that SBP remains unchanged, both in young (Beetham & Buskirk, 1958; Convertino et al., 1984; Davies et al., 1976; Huber et al., 1988; Matzen et al., 1990; Williams et al., 1988) and elderly (Kenny et al., 1987; Lee et al., 1966; Lye et al., 1990) subjects. Two cross-sectional studies comparing the BP response to head-up tilt in young, middle-aged, and elderly subjects also did not find age-related differences. Kaijser and Sachs (1985) evaluated the SBP and DBP response to 8 minutes of 60° tilt and found no difference in response among the groups. Similarly, Smith et al. (1984) found that the MAP response did not differ among different age groups in response to tilt. However, Vargas et al. (1986) found that SBP decreased and DBP increased during 70° head-up tilt in both old and young subjects, with young subjects showing greater increases in DBP. Peripheral resistance increased equally for young and old subjects. In contrast, Dambrink and Wieling (1987) found that SBP decreased in older subjects but remained stable in young subjects during an upright tilt. However, the age-related DBP response was in agreement with Vargas et al. (1986). Similarly, Lipsitz, Maddens, Pluchino, Schmitt, and Wei (1986) found that the peripheral resistance response to standing was greater in young, as compared with old subjects, after one minute of standing. Equivalent responses after three minutes suggested a delay in the vasoconstrictor response in older subjects. Other studies (Ebert et al., 1982; Frey & Hoffler, 1988; Jansen et al., 1989; Shannon et al., 1991) finding that DBP and/or

peripheral resistance increases more in older subjects have attributed the enhanced response to a compensatory mechanism for the decreased HR and \dot{Q} response.

Few longitudinal studies document the cardiovascular responses to tilt after a period of physical training but several have addressed the issue of training-induced responses to tilt by comparing trained and untrained subjects in a cross-sectional design. Diaz and Rivera (1986) showed that trained subjects had a significantly lower HR both during supine rest and during a 30-minute tilt. During the tilt, trained subjects increased HR by 17 beats•min⁻¹ while untrained subjects increased HR by 24 beats•min⁻¹. This may be related to training-induced hypervolemia. Klein, Wegmann, Bruner and Vogt (1969) and Klein, Bruner, Jovy, Vogt, and Wegmann (1969) also found that trained subjects had lower HRs under both rest and tilt conditions. While the magnitude of the change from rest to tilt reported by Klein, Wegmann, Bruner and Vogt (1969) was 6.2 beats•min⁻¹ lower in the trained subjects, the relative increases were nearly identical (33.7% vs. 32.3% beats•min⁻¹ for trained and untrained subjects, respectively). Similarly, Harma and Lansimies (1985) did not find a difference between fit and untrained men in the relative magnitude of the HR response to tilt.

In an early longitudinal study, Beetham and Buskirk (1958) found that physical conditioning did not change the HR or BP response to 70° tilt in young subjects. On the other hand, Shvartz et al. (1981) found a lower HR and better maintenance of BP during tilt table testing in 5 of 10 subjects after training and/or heat acclimation. However, the lack of a true control (non-exercising) group in this study does not permit definitive conclusions to be made regarding the effects of training alone. Improved responses to 60° tilt were also found by Convertino et al. (1984) after 8 days of cycle ergometer

training at 65% of $\dot{V}O_2\text{max}$. Mean tilt duration to syncope increased by 6 minutes, associated with an increase in PV and a decrease of 9 beats $\cdot\text{min}^{-1}$ in the HR response to tilt. However, the heart rate acceleration from supine to tilt positions only declined 4 beats $\cdot\text{min}^{-1}$ due to a 5 beats $\cdot\text{min}^{-1}$ reduction in resting HR. The BP response to tilt was unchanged by training.

The HR response to tilt after training in elderly individuals has not been characterized. However, there are some animal data to suggest that exercise training increases NE content in the heart (Gwathmey et al., 1990); this may indicate an increased adrenergic responsiveness. Whether this would result in an increased HR response during tilt is not known; confounding factors might include increases in SV and/or BV, which would tend to offset any increase in HR.

Blood/Plasma Volume

Hagan, Diaz, and Horvath (1978) studied the effect of 35 minutes of supine posture, followed by 35 minutes of standing, on Hct, Hb concentration, plasma PROT, and PV in young subjects. After 35 minutes in the supine posture, PV increased by 440 ml, representing an increase of 11.7%. Assumption of the standing position resulted in an increase of 10.3% and 10.8% for Hct and Hb, respectively, and an increase of 20.8% in plasma proteins. Hydrostatic pressure produced a fluid efflux of 593 ml and reduced BV and PV by 9.5 and 16.2%, respectively. Red cell mass was unchanged by posture. Davies et al. (1976) found similar results in a 45-minute, 85° tilt. After 45 minutes, PV had decreased 16.8%, with a corresponding increase in Hct of 11%, from 41.0 to 45.5.

A 2-hour, 45° head up tilt induced a significant increase in Hct from 42.5 to 44.0, resulting in a calculated decrease in PV of 7.2% in young subjects

(Williams et al., 1988). Tarazi, Melsher, Dustan, and Frohlich (1970), however, found somewhat smaller PV decreases during a 20-minute, 50° tilt. Their subjects experienced a PV decrease of 113 ml, corresponding to a 3.9% decrement. Data from studies with the elderly demonstrate results similar to the majority of studies with young subjects. Lye et al. (1990) found that a 10-minute, 70° head-up tilt elicited a 10.8% decrease in PV in healthy elderly subjects.

Physical training does not appear to affect the magnitude of the PV decrement during tilt. Convertino et al. (1984) found that although the absolute PV decrease during a 60° tilt was greater after 8 days of training (544 ml vs. 479 ml), the relative decrement remained the same (13.9% vs. 13.6%). Similar results were found by Greenleaf et al. (1988) who studied the response to a 60° head-up tilt before and after a 6-hour water immersion protocol both prior to and after 6 months of exercise training in young to middle-aged men. Plasma volume decreases ranged from 9.0% to 12.6% during the four tilt procedures. In addition, neither pre- nor post-tilt Hb and Hct values were changed with training. Hemoglobin increased from 14.5 to 15.8 while Hct increased from approximately 37.0 to 39.9 during tilt both pre- and post training.

Vasoactive Hormones

Vasopressin (AVP). Upright posture translocates approximately 500 ml of blood to the lower extremities while another 200-300 ml may be transferred to the veins in the buttocks and pelvis (Blomqvist & Stone, 1983); prolonged tilt further reduces BV by filtration of plasma from the capillaries in the legs. This decrease in central BV and CVP may promote AVP secretion through stimulation of cardiopulmonary receptors (Harrison et al., 1986).

That AVP secretion during tilt is stimulated by volume receptors is supported by research showing that dehydration results in greater resting and tilt AVP concentrations. Harrison et al. (1986) found that resting levels of AVP were five times higher, while tilt values were approximately 6.5-7 times higher in dehydrated subjects. Similarly, Greenleaf et al. (1988) found that AVP levels were increased in response to tilt after, but not before, a 6 hour water immersion which reduced body weight by 1.12 kg.

Vasopressin secretion during head-up tilt may also be affected by increases in the renin-AII axis resulting from generalized sympathetic stimulation, decreased renal blood flow and/or pressure, or decreased osmolar load at the juxtaglomerular cells (Mouw, Bonjour, Malvin, & Vander, 1971; Ramsay, Keil, Sharpe, & Shinsako, 1978). Hypotension is also a potent stimulator of AVP secretion (Share, 1976).

Vasopressin promotes homeostasis during orthostasis by increasing the permeability of cells in the collecting ducts to water, thus increasing the reabsorption of fluid in the kidney. Vasopressin also limits filtration of plasma into the interstitial space by the selective vasoconstriction of skeletal muscle and skin arterioles. The result is both a redistribution of vascular volume to critical tissues (e.g., the brain), and a lowering of capillary pressure which favors net reabsorption of fluid from the interstitial space. The increased peripheral resistance induced by AVP does not usually increase BP because of baroreceptor-induced compensatory changes in HR and \dot{Q} . In addition, AVP may cause a reduction in cardiac contractility as a result of coronary arteriolar constriction (Goodman & Frey, 1988).

Many researchers have documented the expected increase in AVP during tilt. However, increases from basal values appear to vary widely, ranging from 25 to 175% (Davies et al., 1976; Huber et al., 1988; Lye et al., 1990;

Sander-Jensen et al., 1986; Williams et al., 1988). Davies et al. (1976) found that tilt values were approximately 1.6-1.9 times higher than basal values up to a tilt duration of 30 minutes, after which time AVP increased strikingly to 3-4.5 times basal values. This occurred when HR and BP were stable but when PV had reached its nadir (-17%). These data support the role of volume receptors in regulating AVP during postural stress. Davies, Forsling and Slater (1977) also documented large increases (approximately 700%) in AVP release only after 30 minutes of tilt and hypothesized that the delayed increase was due to the increase in renin and AII.

Basal values of AVP may be higher in the elderly but the magnitude of increase during tilt may not differ between young and old (Vargas et al., 1986). The increase in AVP secretion is most likely due to volume receptors since osmolality generally remains constant (Greenleaf et al., 1988; Harrison et al., 1986; Sander-Jensen et al., 1986); however, hyperosmolality cannot be disregarded since it has been shown to increase (Vargas et al., 1986).

Differences among studies attempting to document the AVP response of elderly and young subjects may be due to the existence of "responders" and "nonresponders". Rowe, Minaker, Sparrow, and Robertson (1982) found that some subjects did not increase AVP during 8 minutes of quiet standing, and that the prevalence of "nonresponders" increased with age from 8.3% (1 of 12) in young subjects to 46.7% (7 of 15) in elderly subjects.

Despite the presence of appropriate stimuli and the apparent beneficial effects of AVP in maintaining BP homeostasis, not all studies have documented AVP increases during tilt. Mohanty et al. (1985) found that AVP did not increase in young to middle-aged subjects during a 5-minute, 80° head-up tilt. These authors suggested that AVP is not secreted in response to LBNP or tilt unless significant hypotension occurs. Indirect support for this

hypothesis is offered by Ecoffey et al. (1985) who found that AVP did not change in elderly men during tilt when MAP remained constant. However, the low angle of tilt (30°) may be responsible for the nonresponsiveness of the neurohumoral system. Bie, Secher, Astrup, and Warberg (1986) found unchanged AVP during 20° and 40° tilts associated with unchanged or increased MAP. Although MAPs were not reported, both Banner et al. (1990) and Greenleaf et al. (1988) also found no change in AVP during tilt protocols utilizing 45° and 60° angles, respectively.

The data regarding the AVP response to tilt after physical training are not entirely consistent. Greenleaf et al. (1985) found that AVP increased during tilt before, but not after, a 12-day heat acclimation/exercise program. Convertino et al. (1984) also found a decrease in the AVP response to a 60° tilt after 8 days of training. Compared with the response prior to training, the peak AVP response declined 37.7%; however, this was not found to be statistically significant. A decline in the AVP response to tilt after training is consistent with the hypothesis that a training-induced increase in PV better maintains central BV and pressure (Convertino et al., 1984).

In contrast, Greenleaf et al. (1988) found that AVP levels did not increase during a 60° tilt either before or after 6 months of training. However, both pre- and post-training values of AVP were significantly increased by an identical tilt protocol after 6 hours of water immersion, lending support to the hypothesis that AVP secretion is not stimulated by reductions in central BV until PV losses reach approximately 20%.

Renin (PRA). Renin release from the JG cells in the kidney is stimulated by decreases in arterial pressure and the AII-mediated increase in arteriolar vasoconstriction and peripheral resistance raise arterial pressure back to normal. AII also excites sympathetic vasomotor outflow, thus

reinforcing its own vasoconstrictor action. In addition, AII increases cardiac contractility by increasing calcium influx in cardiac myocytes. The combination of these effects markedly increases BP and makes AII a potent pressor agent. AII also contributes to maintenance of salt and water balance through the stimulation of both ALDO and AVP secretion (Davies et al., 1977; Goodman & Frey, 1988).

Because of its indirect role in BP and fluid volume homeostasis, renin is increased during tilt, stimulated by high- and low-pressure baroreceptors and through β -receptor-mediated mechanisms (Grassi et al., 1988; Kiowski & Julius, 1978). Upright PRA values average $1.9 \text{ ng AI} \cdot \text{ml}^{-1} \cdot \text{hr}^{-1}$, compared with $1.1 \text{ ng AI} \cdot \text{ml}^{-1} \cdot \text{hr}^{-1}$ for resting values (Thomas, 1985). Like AVP, however, the increments during tilt appear to vary widely. In general, it appears that longer tilt durations elicit greater PRA concentrations, even when the tilt angle is low. A 74% increase was shown by Banner et al. (1990) after a 60-minute, 45° tilt, while Davies et al. (1976, 1977) found increases of 60-80% during 30 minutes of 85° tilt. Increases of 110-120% were found with a 2 hour, 45° protocol (Williams et al., 1988) and with a 25 minute upright protocol (Solomon et al., 1986). In contrast, Mohanty et al. (1985) found only a 44% increase in young to middle-aged subjects during a 5-minute, 80° tilt while Lye et al. (1990) saw a 50% increase in PRA in elderly subjects during a 10-minute, 70° head-up tilt. One exception to this generalization was the 110-120% increase shown by Huber et al. (1988) with a 10 minute upright tilt.

Most authors have found that supine and orthostatic PRA values decline with age (Cleroux et al., 1989; Crane & Harris, 1976; Hayduk et al., 1973; Saruta et al., 1980). The relative increases during tilt, however, may be similar between young and old subjects, averaging 100% across the age range (Hayduk et al., 1973). The decrease in renin release with age may be due to a

decrease in cardiopulmonary baroreceptor sensitivity. Cleroux et al. (1989) found that elderly subjects did not increase renin activity during LBNP despite significant decreases in CVP, while young and middle-aged subjects demonstrated significant increases in PRA with equivalent changes in CVP. Ecoffey et al. (1985) and Kenny et al. (1987) also found that PRA did not increase in elderly individuals during tilt. However, the low tilt angles used in these studies may have affected the results: Ecoffey et al. (1985) used a 15-minute, 30° head-up tilt in elderly men, while Kenny et al. (1987) utilized a 2-hour, 40° tilt in asymptomatic elderly men and women. Gender differences may also have affected the renin response to orthostasis in the Kenny et al. (1987) study. Gregerman and Bierman (1981) state that in one-third of females over the age of 70, renin activity levels are not only low but fail to rise with postural change. The use of a combined sample of males and females may have masked a possible tilt-induced increase in the elderly males.

The PRA response to tilt after training is potentially important since it may be a primary mechanism for the increase of peripheral resistance through AII formation. A decrease in the peripheral resistance response to orthostasis as a result of endurance training has been proposed as a mechanism of reduced orthostatic tolerance in trained subjects (Goldwater, DeLada, Polese, Keil, & Luetscher, 1980; Mangseth & Bernauer, 1980). However, the data are scant and contradictory. On the one hand, Greenleaf et al. (1988) found that PRA increased in response to a 60° tilt prior to, but not after 6 months of exercise training in young and middle-aged men. In contrast, Convertino et al. (1984) found that 8 days of training did not change the peak PRA response to a 60° tilt.

Catecholamines. Increases in SNS activity and plasma NE levels as a result of orthostasis are well-documented (Cryer, 1980; Jansen et al., 1989;

Mohanty et al., 1985; Vargas et al., 1986; Williams et al., 1988; Zerbe, Henry, & Robertson, 1983). Increases can range from a low of 60-80% (Banner et al., 1990; Jensen et al., 1989; Sander-Jensen et al., 1986; Williams et al., 1988) to 150-170% (Cleroux et al., 1989; Huber et al., 1988). Although some researchers have found that NE levels are greater at rest (Gregerman & Bierman, 1981; Jensen et al., 1989; Vargas et al., 1986) and during tilt (Vargas et al., 1986) in elderly subjects when compared to young subjects, Cleroux et al. (1989) found similar resting NE levels in young (16-30 years), middle-aged (37-49 years) and elderly (61-73 years) subjects. However, Cleroux et al. (1989) found that the NE response to an equivalent drop in CVP induced by LBNP was significantly less in elderly subjects, and attributed this decline to a reduction in the sensitivity of the cardiopulmonary baroreceptors. A reduction in NE secretion in response to tilt in the elderly is also suggested by comparing the results of Sander-Jensen et al. (1986) and Ecoffey et al. (1985). In the former study, a significant increase in NE was found in response to a 30° tilt in young subjects, while in the latter study, no increase in NE was found in 58 to 82 year old men during a 15-minute tilt at the same angle.

The basal function of the adrenal medulla does not appear to change with age; thus resting levels of EPI remain constant (Gregerman & Bierman, 1981). Low angles of tilt (e.g., 30°) do not appear to stimulate EPI secretion either in young (Sander-Jensen et al., 1986) or old (Ecoffey et al., 1985) subjects. In contrast, greater angles of tilt (e.g., 45° and 60°) stimulated EPI secretion in young subjects (Banner et al., 1990; Sander-Jensen et al., 1986). The effect of tilt duration is less clear. Although some researchers using protocols of 5 and 10 minutes (Mohanty et al., 1985; Huber et al., 1988) did not find significant changes in EPI, Jansen et al. (1989) found similar increases (approximately 85%) in young and old subjects in a 10-minute, 45° head-up tilt.

There are scant data characterizing the catecholamine response to tilt after training. The only data appear to be from a heat acclimation/exercise study by Greenleaf and coworkers (1985); it was found that EPI and NE did not increase in response to a 70° head-up tilt test prior to 12 days of heat acclimation and exercise. However, increases were noted during the tilt test at the end of the 12-day study. The response of elderly individuals after training has not been studied.

Summary. Vasopressin, renin, and NE all act to maintain BP homeostasis during orthostasis via a variety of mechanisms. Although increases in these hormones during head-up tilt have not been universally documented, differences in protocols may account for some of the discrepancies.

Hormones Associated with Fluid Volume Control: Aldosterone (ALDO)

Increased ALDO causes an increase in the reabsorption of Na⁺ and water and an increase in the excretion of K⁺ in the renal collecting ducts. Because of its role in defending BV, head-up tilt increases, while supine posture inhibits, ALDO. Upright ALDO levels average 30-280 pg•ml⁻¹ (Loriaux & Cutler, 1986), compared with 20-100 pg•ml⁻¹ for supine values (Labhart, 1986).

While some investigators have indeed found an increase in ALDO during head-up tilt (Bie et al., 1986; Mohanty et al., 1985; Sander-Jensen et al., 1986; Vargas et al., 1986), other investigators have found increases in ALDO during tilt only under pathological conditions. For example, Harrison and coworkers (1986) found that tilt-induced ALDO secretion occurred only during dehydration. Similarly, neither Sander-Jensen and coworkers (1986) nor Huber et al. (1988) found ALDO increases during head-up tilt until pre-syncopal symptoms became evident.

Although some authors have found that aging decreases resting plasma levels of ALDO due to a concomitant decrease in PRA (Crane & Harris, 1976; Saruta et al., 1980), Vargas et al. (1986) found that there was no age difference between young and elderly subjects in resting ALDO values. In addition, both age groups increased ALDO secretion to the same extent during a 10-minute, 70° head-up tilt. Both resting and tilt findings are consistent with their data on the renin response. In contrast, Lye et al. (1990) did not find a significant increase in plasma ALDO concentration in elderly subjects as a result of an identical tilt protocol.

Data on the tilt response of ALDO after training are scarce. However, data from a cross-sectional study (Skipka et al., 1979) indicate that the response of ALDO to water immersion may be higher (i.e., less suppressed) in trained subjects, suggesting a decreased sensitivity of cardiopulmonary receptors. There may also be an uncoupling of the renin and ALDO responses with training: Skipka et al. (1979) found that the responsiveness of ALDO secretion did not correspond to renin activity levels, which were not significantly different between trained and untrained subjects at rest and which declined at a similar rate during immersion.

Adrenocorticotrophic Hormone (ACTH)

Because almost any type of physical or mental stress can lead to greatly enhanced ACTH secretion, ACTH levels would be expected to increase during head-up tilt. In addition, ACTH secretion is sensitive to atrial stretch (Cryer & Gann, 1974) so that a decrease in right atrial volume would result in an increased secretion. Several training-induced adaptations would favor a decrease in ACTH secretion during head-up tilt after training. First, an increased PV would favor a greater fluid volume reserve and a better

maintenance of central BV during orthostasis (Convertino et al., 1984). In addition, a training-induced increase in muscle mass may facilitate venous return and enhance CVP during orthostasis and thus contribute to CVP maintenance.

Only two studies have noted the response of ACTH to orthostasis: one found that there were no changes (Galen, Louisy, Habrioux, Lartigue, & Guezennec, 1988) while the other found an approximate 100% increase (Huber et al., 1988). Both studies utilized an upright tilt position; interestingly, it was the shorter of the two protocols (Huber et al., 1988; 10 minutes vs. 25 minutes) which produced the significant increase in ACTH. No studies have recorded the ACTH response to tilt after a program of physical training in either young or elderly subjects.

Protein (PROT), Sodium (Na⁺) and Potassium (K⁺)

Researchers who have measured Na⁺, K⁺, and/or osmolality during a variety of head-up tilt protocols have generally reported no change (Davies et al., 1977; Harrison et al., 1986; Huber et al., 1988; Mohanty et al., 1985; Sander-Jensen et al., 1986). Mohanty et al. (1985) attribute the constancy of K⁺ to the secretion of NE which, via a β_2 -adrenoreceptor-mediated activation of adenylate cyclase, stimulates the Na⁺/K⁺-ATP-ase that pumps K⁺ into skeletal muscle. When NE secretion during tilt was prevented by bromocriptine administration, there was a significant increase in plasma K⁺ concentration.

Sander-Jensen et al. (1986) found small increases in PROT during both 30° (from 8.27 to 8.63 g•dl⁻¹, 4.3%) and a 60° (8.15 to 8.30 g•dl⁻¹, 1.8%) head-up tilts. Hagan et al. (1978) found larger increases (20.8%; from approximately 6.0 to 7.5 g/dl) in the erect posture, compared with resting, supine values.

Training does not appear to affect the PROT or electrolyte response to tilt in young persons. Greenleaf et al. (1985) did not find that Na^+ or K^+ changed during 70° head-up tilt, either before or after a 12-day heat acclimation program. Greenleaf et al. (1988) also found similar electrolyte responses during a 60° tilt to tolerance before and after a 6-month training program; the only exception appeared to be a significant increase in K^+ during tilt prior to training. Although Greenleaf and coworkers (1985; 1988) found that PROT increased during tilt both before and after training and/or heat acclimation, no direct comparisons were made on whether the magnitude of increase was similar at the two time points. Data on the PROT or electrolyte response to tilt after training in older persons are lacking.

Mechanisms Potentially Responsible for Changes in Orthostatic Responses

Plasma Volume Changes

One hypothesis regarding improvements in orthostatic responses after training postulates that an increased BV helps in maintaining orthostatic integrity by providing a larger fluid volume reserve against which fixed gravitational forces act (Blomqvist and Stone, 1983, Bungo, Charles, & Johnson, 1985; Convertino et al., 1984; Hyatt and West, 1977; Shvartz et al., 1981). Convertino et al. (1984) and Shvartz et al. (1981) both document that decreases in orthostatic HR were related to increases in BV. Conversely, Harrison, Kravik, Geelen, Keil, & Greenleaf (1985) documented a relationship between a smaller BV and a tendency to faint during orthostatic maneuvers.

However, two studies provide evidence against this hypothesis. Convertino, Sather, Goldwater, and Alford (1986) studied the effect of various

physical and physiological variables on peak LBNP tolerance. Blood volume contributed to LBNP tolerance in a multiple regression model but the slope was negative, indicating that a high BV was associated with a lower LBNP tolerance. Levine et al. (1991) also found that the subjects with the lowest LBNP tolerance had the greatest resting PV. They speculated that the mechanism responsible for this apparent anomaly might involve a training-induced increase in left ventricular compliance; this would result in greater decreases in EDV and SV for a given reduction in EDP during orthostasis and negate the advantage of an increase in BV.

Paradoxically, the increase in BV together with the parallel increase in CVP (Convertino et al., 1991) may serve to produce a resetting of the low-pressure cardiopulmonary baroreceptors. This allows an increased fluid volume at equivalent hormonal levels. There may also be an attenuation of the cardiopulmonary receptor stimulus-response mechanism leading to a reduction in AVP or renin secretion for an equivalent CVP decrement during orthostasis (Convertino et al., 1984; Greenleaf et al., 1988). An attenuated hormonal response may result in a reduction in the cardiac output or peripheral resistance response to orthostasis. Since higher levels of PRA and AVP during orthostasis appear to play a major role in maintaining tolerance (Harrison et al., 1985; Sather et al., 1985; Sather, Goldwater, Montgomery, & Convertino, 1986; Shvartz et al., 1981), a reduced response would be counterproductive.

Muscle Mass Changes

An increased muscle mass, particularly of the lower body, may help improve orthostatic tolerance due to the enhancement of venous return (Convertino, 1987; Greenleaf et al., 1975). This, in turn, may help to maintain

\dot{Q} and arterial pressure during orthostasis. Postural hypotension in response to simulated microgravity has been associated with decreased musculature, particularly in the lower extremities, and increased compliance in the leg vasculature (Convertino et al., 1989; Duvoisin et al., 1989). Early training studies (Shvartz, 1968a; Shvartz, 1969) suggested that resistance training improved chronotropic responsiveness to standing or head-up tilt. However, it could not be determined whether the improved responses were due to increases in muscle mass or changes in baroreceptor sensitivity.

Changes in Baroreceptor Sensitivity

High-pressure baroreceptors in the carotid sinus and aortic arch are mechanoreceptors sensitive to changes in arterial pressure. A fall in arterial pressure, such as is induced during orthostasis, decreases afferent nerve activity and releases inhibitory activity in the cardiovascular centers of the central nervous system. A series of reflexes ensue which act to maintain arterial pressure by increasing \dot{Q} and/or peripheral resistance. The end result is an increase in HR and contractility, increased veno- and vasoconstriction, and reduced blood flow to the skin, skeletal muscles, kidney and splanchnic area (Convertino, 1987).

The effect of physical conditioning on baroreflex sensitivity is a controversial issue, partially due to the use of different experimental designs (cross-sectional vs. longitudinal). An early cross-sectional study by Stegemann, Busert, and Brock (1974) found that the HR and BP responses to both neck suction and neck pressure were less in trained runners than in sedentary controls. In later studies, endurance athletes were found to have a lesser baroreflex sensitivity during LBNP compared with resistance trained athletes (Smith et al., 1988; Smith & Raven, 1986) or untrained subjects

(Raven, Graitzer, Smith, & Hudson, 1985; Raven, Rohm-Young, & Blomqvist, 1984). In contrast, Barney et al. (1985) found that young endurance trained men had increased baroreceptor responses to neck suction when compared to untrained men. Finally, some cross-sectional studies provide evidence that training does not affect the baroreflex. Falsetti, Burke, and Tracy (1982) found that the HR responses of trained swimmers and untrained controls to neck suction and neck pressure were similar. In addition, MAP responses of the two groups to LBNP were not significantly different. Hudson, Smith and Raven (1987) also found that baroreflex sensitivity at -50 mmHg of LBNP was similar for trained and untrained women. Levine et al. (1991) found similar baroreflex responses in high-, mid-, and low-fit young men in response to neck suction and neck pressure. Finally, Fiocchi, Fagard, Vanhees, Grauwels, and Amery (1985) found that baroreflex sensitivity did not correlate with $\dot{V}O_2\text{max}$ in trained cyclists. However, the low correlation ($r = 0.05$) may be partly due to the homogeneity in the $\dot{V}O_2\text{max}$ values ($54.1 \pm 1.4 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$).

Longitudinal animal data provide equally equivocal results. Tipton, Matthes, and Bedford (1982) and Bedford and Tipton (1987) provide animal data in support of the hypothesis that endurance training attenuates baroreflex control of BP, particularly during hypotensive episodes. In their experiments, trained rats experienced greater and faster falls in arterial pressure during LBNP than untrained controls; the group differences were abolished with baroreceptor denervation. The data from Gwartz, Brandt, Mass, & Jones (1990), using a dog model, support this conclusion. However, in an earlier study, this group of investigators (Mass, Gwartz, Smith, & Umeakunne, 1986) found that baroreceptor sensitivity in dogs was not affected by 10 weeks of daily exercise training.

Longitudinal training data in humans is scarce. Somers, Conway, Johnson, & Sleight (1991) reported that 6 months of endurance training in middle-aged hypertensives resulted in an increase in baroreceptor sensitivity as measured during phenylephrine infusions. This was accompanied by decreases of 9.7 and 6.8 mmHg in systolic and diastolic pressures, respectively, a prolongation of the R-R interval, and an increase in the R-R variability. They noted, however, that hypertension is associated with a decrease in baroreceptor sensitivity and a decrease in the R-R variability, and that these appeared to normalize with training. Whether normotensive individuals would see the same changes was not investigated.

In contrast, Seals and Chase (1989) suggest that training has no effect on baroreceptor responsiveness. They found that 11 weeks of endurance training in middle-aged and older men did not alter the baroreflex control of HR in response to neck suction, neck pressure, or LBNP. Similarly, Vroman, Healy, & Kertzer (1988) report that 12 weeks of endurance training in young men produced no change in the baroreflex sensitivity (as measured by $\Delta\text{HR}/\Delta\text{SBP}$) during LBNP at -40 mmHg. While baroreflex sensitivity decreases with age (Gribbin et al., 1971; Lipsitz, 1989), the effect of training on this parameter has not been investigated.

Altered Hormonal Response

The response of vasoactive hormones to orthostasis may be affected by training if low- and/or high-pressure baroreflex sensitivity is altered. Although basal AVP secretion does not appear to change with training (Convertino et al., 1980a; Convertino et al., 1983; Convertino et al., 1991), it is possible that training attenuates the response of the cardiopulmonary receptors to acute changes in CVP (Boning & Skipka, 1979; Claybaugh et al.,

1986; Skipka et al., 1979). A reduction in resting (Hagberg et al., 1989b; Kiyonaga et al., 1985) and orthostatically-induced (Goldwater et al., 1980) NE secretion after training may be a mechanisms for reducing renin secretion after training (Davies et al., 1977).

Changes in vascular sensitivity to pressor hormones may also play a role in altering responses to orthostasis. Wiegman et al. (1981) found decreases in vasoconstrictor, and possibly venoconstrictor, response to NE after 6 weeks of endurance training in rats, and hypothesized (Wiegman, 1981) that β -adrenergic sensitivity was increased. This could play a role in altered BP and peripheral resistance responses during orthostasis.

Summary

Physiological responses hypothesized to contribute to the maintenance of arterial pressure during orthostasis are altered by physical training. The direction of change, however, is not always consistent with an improvement in the orthostatic responses, when each mechanism is considered separately. Blood volume increases may provide a larger fluid volume reserve to offset fluid translocation during orthostasis; however, the effect of this larger volume may be to reduce cardiopulmonary baroreceptor sensitivity and vasoactive hormone release. The chronotropic responsiveness of the high-pressure baroreceptors may also be attenuated; this may be offset somewhat by a larger BV and an improved SV. Finally, training may improve muscle mass and tone and thus improve responses to orthostasis via an improved venous return.

CHAPTER 3 METHODOLOGY

Subjects

Eighty-three subjects, ranging in age from 60 to 82 years, volunteered to participate in this study. An initial screening by telephone was used to identify subjects who were within the desired age range, had been sedentary for at least one year, and who had no overt history of cardiovascular or pulmonary disease, or any orthopedic limitations to exercise testing and training. Subjects meeting these criteria reported to the laboratory where the entire study protocol, the inherent risks and hazards of the study, and the necessary time commitment were explained. Subjects were also asked to complete demographic, medical history, and activity questionnaires (Appendix A). These forms were reviewed by the investigator; subjects not meeting the physical and health requirements for the investigation were notified and excluded from the study. Subjects meeting the requirements were scheduled for a further screening visit. Written informed consent was obtained from each subject who wished to continue (Appendix B). Based on this orientation, eight subjects were disqualified due to prior cardiac disease ($n = 5$) or other medical or orthopedic problems ($n = 3$). Ten subjects elected not to continue. All procedures were approved by the University of Florida College of Medicine Institutional Review Board (Appendix C).

In a separate screening visit, the subject's medical history questionnaire was reviewed by a physician; the physician then administered a

cardiovascular physical examination, including a resting 12-lead electrocardiogram (ECG). If any clinically significant findings such as hypertension (blood pressure [BP] exceeding 160/100 mmHg at rest), angina pectoris, or an abnormal resting ECG (ST segment depression or elevation that is horizontal or downsloping greater than 1 mm, 0.08 seconds from the J-point, or the presence of abnormal Q waves) were found, the subject was referred to his/her personal physician and excluded from participation in the study.

Subjects that were deemed suitable were then administered a graded treadmill exercise test (GXT) according to the Naughton protocol (Naughton & Haider, 1973). The protocol used a constant speed of 2 miles•hour⁻¹; the grade was 0% initially and increased 3.5% every 2 minutes. The test continued until the subject reached voluntary maximal exertion or became symptomatic with positive hemodynamic or medical indices. Heart Rate (HR) and ECG were monitored continuously throughout the exercise and recovery periods. A 12-lead ECG was recorded at the end of each stage of exertion, at peak exercise, and at each minute for 7 minutes of recovery; a 3-lead ECG rhythm strip was recorded at the intermediate minute of each exercise stage. Blood pressure was measured by auscultation at rest prior to exercise, at the end of each stage of exercise, immediately post-exercise, and at minutes 1, 3, 5, and 7 of recovery. Rating of perceived exertion (RPE) using the Borg scale (Borg, 1982) was determined during each minute of exercise.

For subjects to continue in the study, the test must have been terminated by the subject because of fatigue with no significant evidence of hemodynamic or cardiorespiratory problems. The test was terminated by the investigators and/or attending physician if any of the following occurred: angina pectoris, ataxia or pallor, symptomatic supraventricular tachycardia,

horizontal or downsloping ST segment depression that was greater than 3 mm at 0.08 seconds after the J-point, second or third degree heart block, onset of bundle branch block, ventricular couplets ($> 2/\text{min}$), ventricular tachycardia (≥ 3 consecutive PVC's), R on T premature ventricular contractions (PVCs), frequent unifocal PCVs ($>10/\text{min}$), frequent multifocal PVCs ($>4/\text{min}$), a BP in excess of 250/110, or a drop in systolic BP (American College of Sports Medicine, 1991). All GXTs were supervised by a physician trained in cardiovascular exercise testing. A crash cart with all necessary emergency medications and a defibrillator was immediately adjacent to the treadmill during every GXT.

Based on the physical examination and GXT, 21 subjects were disqualified from further participation in the study. Reasons for disqualification included elevated resting BP ($\underline{n} = 5$), other resting ECG abnormalities ($\underline{n} = 2$), abnormal HR or BP response to exercise ($\underline{n} = 4$), and ST segment depression during exercise ($\underline{n} = 10$). Thus, 44 subjects (14 males, 30 females) were accepted into the study.

Type of Data Needed

The criterion measures indicative of the cardiovascular response to an orthostatic stress were the HR, stroke volume (SV), cardiac output (\dot{Q}) and BP responses during a 30-minute supine rest; a 15-minute, 70° head-up tilt; and a 15-minute supine recovery. These responses were recorded during initial (T1) testing and also at the midpoint (13 weeks; T2) and end (26 weeks; T3) of a physical training program (Appendix D).

Several mechanisms have been proposed to explain improvements in the cardiovascular response to an orthostatic stress after training. These mechanisms include a) an increased blood volume (BV), b) improved

baroreflex function, c) increased muscle mass, and d) improved hormonal response. An appropriate analysis of each mechanism was needed to determine which factor, if any, contributed to improved orthostatic responses. Blood volume was measured at T1 and T3 using the Evan's Blue dye technique (Greenleaf et al., 1979) while baroreflex responsiveness was assessed by analyzing the HR response to coughing in the supine and 70° tilt positions (Cardone et al., 1987; Maddens, Lipsitz, Wei, Pluchino, & Mark, 1987; Wei & Harris, 1982). Lower body muscle mass was assessed using dual x-ray absorptiometry (Haarbo, Gotfredsen, Hassager, & Christiansen, 1991).

Increases in vasoactive hormones in response to upright tilt act to maintain blood pressure. Therefore, the levels of vasopressin (AVP), plasma renin activity (PRA), norepinephrine (NE) and epinephrine (EPI) were assessed at rest and during upright tilt. Other hormones and electrolytes instrumental in fluid volume control and the stress response (adrenocorticotrophic hormone [ACTH], aldosterone [ALDO], sodium [Na⁺], potassium [K⁺], and protein [PROT]) were also measured at rest and during tilt. Finally, data from a maximal oxygen uptake test and strength tests were used to assess the presence and magnitude of the training response.

Methods of Data Collection

Maximal Oxygen Uptake ($\dot{V}O_{2\max}$) Test

Prior to testing, a 20 or 22 gauge, 1 1/2 inch venous catheter was placed under aseptic conditions in an antecubital vein for blood sampling to determine plasma hormones (ACTH, AVP, PRA, ALDO, EPI, NE), plasma PROT, and electrolytes (Na⁺ and K⁺) at rest and at maximal exercise. The catheter was kept patent during the test with sterile heparinized saline.

Subjects rested in the supine position for 20 minutes after catheter placement before a 24-26 ml blood sample was drawn for determination of resting hormones, PROT, and electrolyte values. The blood sample was divided among pre-chilled vacuum-type collection tubes (Vacutainer, Becton-Dickinson, Rutherford, NJ) containing ethylenediaminetetracetic acid (EDTA) (for ACTH, AVP, PRA, ALDO), or heparin/EGTA/glutathione (for PROT, electrolytes, EPI, NE). The samples were centrifuged at 3500 rpm for 15 minutes at 2-4° C. The plasma was placed into separate polypropylene tubes and kept frozen at -20° C (ACTH, AVP, PRA, ALDO, PROT, electrolytes) or -80° C (NE, EPI) until analysis.

The subject then performed a symptom limited maximal treadmill test to determine peak oxygen consumption. The test consisted of the Naughton protocol; however, if the subject walked for longer than 12 minutes during the initial screening GXT, the initial speed during the $\dot{V}O_{2\max}$ test was 3 miles•hr⁻¹, rather than 2 miles•hr⁻¹. During the $\dot{V}O_{2\max}$ test, the subject breathed through a mouthpiece attached to a low-resistance breathing valve and had a nose clip in place; expired air was collected in meteorological balloons. The expired air was analyzed for fractional oxygen and carbon dioxide concentrations using gas analyzers (Ametek-Thermox, Pittsburgh, PA) calibrated with precision gases. Expired gas volumes were measured with a 120 liter Tissot spirometer (Collins, Braintree, MA).

During the $\dot{V}O_{2\max}$ test, the subject's HR, ECG, BP, and RPE were monitored in the same manner as during the screening GXT, and the same signs and symptoms used for stopping the GXT prior to the subject's achieving volitional maximal exertion were also used. Immediately upon cessation of exercise, another 24-26 ml venous blood sample was drawn and treated as for the resting sample. Testing at T2 and T3 was identical to the

initial $\dot{V}O_2\text{max}$ protocol except that blood samples were not taken at T2. Ambient temperature during the test was kept at 23-24°C.

Tilt Table Test

Preparation for testing included the placement of ECG electrodes (for monitoring standard and augmented limb leads), and mylar-coated aluminum electrode tapes around the neck and thorax (for monitoring HR, SV and \dot{Q}). A 20 or 22 gauge, 1 1/2 inch venous catheter was placed under aseptic conditions in an antecubital vein for a) PV measurement, and b) blood sampling to determine plasma hormones, PROT, electrolytes, Hb and Hct before and after the tilt procedure. The catheter was kept patent during the entire test period with sterile heparinized saline. A small (approximately 1 ml) venous blood sample was taken at the time of the catheter insertion for the determination of Hct, which was necessary for the calculation of SV with the impedance cardiograph.

The subject assumed a supine position on the motorized tilt table (Model 720, Tri W-G, Inc., Valley City, ND) and was connected to ECG (Quinton, Seattle, WA) and cardiac impedance (Minnesota Impedance Cardiograph, Model 304B, Surcom, Inc., Minneapolis, MN) monitoring devices. A BP cuff was fitted around the upper arm for manual BP measurement. Heart rate, SV, and BP were measured during a 30-minute supine control period after 15, 20, 25 and 30 minutes. Stroke volume was measured with the impedance cardiograph using three representative waveforms during the first 15-20 seconds of each measurement period. Heart rate was measured as the instantaneous rate obtained from the same R-R intervals as the SV measurements. The mean of the three measurements was taken as the representative value for each measurement period. Cardiac

output was calculated by the impedance cardiograph as the product of HR and SV. Systolic and diastolic BP were measured manually with a mercury sphygmomanometer (PyMoh, Somerville, NJ) and stethoscope after the impedance measurements were made. A digital readout of the HR was continually available on the ECG monitor and a 6-second rhythm strip was recorded along with the cardiac impedance measurements. A 24-26 ml venous blood sample was drawn after approximately 28 minutes of supine rest for the duplicate determinations of plasma hormones, PROT, and electrolytes; blood samples were treated as described for the $\dot{V}O_2$ max test. The blood sample for triplicate measurements of Hct and Hb was placed in a pre-chilled EDTA-treated vacuum-type collection tube and placed on ice or refrigerated until analysis.

At the end of 30 minutes of supine rest, baroreflex responsiveness was assessed by the response to coughing (Cardone et al., 1987; Wei & Harris, 1982). A 1-minute baseline period commenced and the BP was measured during the final 30 seconds of this period. The subject was then instructed to cough by inhaling deeply and coughing forcefully 3 times in rapid succession. Blood pressure was measured immediately on cessation of the cough. An ECG strip was recorded continually beginning 10 seconds prior to the cough to provide the baseline R-R interval, and ending 1 minute after cough cessation. The sequence was repeated two more times.

Plasma volume (PV) measurement was then made. For this measurement, a 23 gauge butterfly infusion set was inserted into an antecubital, wrist or hand vein on the arm opposite the one in which the venous catheter was inserted. A known quantity (approximately 2 - 2.5 ml) of a 0.5% aqueous T-1824 (Evan's blue dye) solution was injected over a 90 second interval and a 5 ml blood sample taken via the venous catheter 10

minutes after the injection (Greenleaf et al., 1979). The blood was placed in a heparin-treated vacuum-type collection tube and centrifuged at 3500 rpm for 15 minutes at 2-4° C. The plasma was placed in a polypropylene tube and kept frozen at -20° C until analysis.

After PV determination, the fixed-speed motorized tilt table was brought from supine to the 70° head-up position, taking approximately 15-20 seconds. The 15-minute tilt period began once the subject was in the 70° head-up position (T_0). A HR rhythm strip was recorded every minute during the first 6 seconds of each minute. Impedance measurements were made during the first 15-20 seconds of each minute. Blood pressures were recorded 30 seconds after T_0 and after impedance measurements at minutes 1, 2, 3, 4, 5, 10, and 15. A 24-26 ml venous blood sample was drawn between minutes 13-15 of the tilt procedure and analyzed for Hct, Hb, plasma hormones, PROT, and electrolytes. At the end of the 15-minute tilt, the subject again repeated the cough sequence while in the 70° head-up position.

The tilt test was discontinued if any of the following occurred: a) the subject reached the predetermined time limit for the tilt portion of the test; b) presyncopal symptoms such as a fall in systolic BP greater than 15 mmHg between adjacent 1 minute measurements and/or a sudden bradycardia greater than 15 beats•min⁻¹ occurred; c) the systolic BP fell below 80 mmHg; or d) the subject requested to stop due to dizziness, nausea, or discomfort (Sather et al., 1986).

Following completion or discontinuance of the tilt portion of the test, the subject was returned to the supine position in approximately 15-20 seconds. The 15-minute recovery period began upon reaching the supine position. Measurements (HR, SV, \dot{Q} , BP) were made along the same time schedule as during the tilt. During the entire test, the subject was asked to

refrain from conversation, aside from answering any questions from the investigators regarding their status, and from unnecessary movement.

Temperature during the test was kept at 23-24°C. The tilt test was repeated at T2 and T3 and was identical to the initial test except that PV was not measured and blood samples were not taken at T2.

Strength Testing

One repetition maximum (1-RM) leg strength was assessed using the Nautilus™ (Dallas, TX) Leg Press machine. Arm strength was assessed with the Nautilus™ Biceps Curl machine and the Nautilus™ Triceps Extension machine. Subjects with range-of-motion limitations in the hip, knee, or shoulder were tested by either adjusting the seat position on the machine or by "double pinning" the weight stack. Thus subjects were tested through the pain-free part of their range-of-motion. These variations were recorded so that subjects were tested in the same manner at T2 and T3. Subjects began by warming up with 4-5 submaximal repetitions. The resistance on any subsequent single lift was increased by 5-10 pounds according to the difficulty with which the subject executed the previous lift; a one minute rest was allowed between trials. The 1-RM was considered to be the maximum amount of weight that could be lifted through the subject's pre-determined full range-of-motion.

Lumbar extension strength was assessed with a MedX™ (Ocala, FL) Lumbar Extension machine. Subjects underwent a multiple joint angle test consisting of maximum voluntary isometric contractions at seven angles (0°, 12°, 24°, 36°, 48°, 60°, 72° of lumbar flexion; where 0° represented full extension and 72° represented full flexion). Subjects with range-of-motion limitations were tested only at angles consistent with their capabilities.

Testing always proceeded consecutively from 72° to 0° of flexion. The criterion measure consisted of the maximum strength averaged over the number of angles tested.

Body Composition

Muscle mass was assessed noninvasively using a Dual-Energy X-ray Absorptiometer (Lunar Radiation, Madison, WI). The subject lay in a supine position while the X-ray scanner performed a series of transverse scans moving from head to toe at 1 cm intervals. Measurements of total and regional bone mineral content, fat mass and fat free mass were obtained.

Measurements of skinfold thickness were made with Lange calipers (Cambridge, MA) at the triceps, chest, axilla, subscapula, abdomen, suprailium, and thigh, following the procedures outlined by Pollock and Wilmore (1990). Measurements from the seven sites were summed ($\Sigma 7$). Body circumferences were measured with a steel tape at the shoulder, abdomen, waist, gluteus, right thigh, and right upper arm following the procedures outlined by Pollock and Wilmore (1990).

Blood Sample Analyses

Plasma volume analysis. T-1824 (Evan's blue) dye analysis was based on the methods of Greenleaf et al. (1979). The dye from the plasma sample was extracted onto a wood-cellulose powder (Solka Floc SW-40A) chromatographic column after it had been separated from the albumin by the action of a detergent (Teepol 610 in 2% Na₂HPO₄). Interfering substances such as pigments, proteins, and chylomicrons were washed from the column with 2% Na₂HPO₄. The dye was then eluted from the column with an 1:1 acetone-

water mixture. The addition of KH_2PO_4 buffered the pH of the eluate to 7.0; the absorbance of the eluate was read at 615 nm. Plasma volume was calculated from the formula:

$$\text{PV} = \frac{(\text{VXD})(\text{STXv})}{1.03(\text{T})}$$

where

- V = volume (ml) of T-1824 dye injected (22.6 mg/5 ml)
- D = dilution of standard (1:250)
- St = absorbance of standard
- v = volume of sample extracted (1.0 ml)
- T = absorbance of plasma sample
- 1.03 = correction factor for dye uptake by tissues

BV was calculated as $\text{PV}/(1 - 0.91\text{Hct})$.

Hemoglobin; hematocrit. Hemoglobin (Hb) concentration was determined with triplicate measurements using the cyanmethemoglobin method (Sigma Diagnostics, St. Louis, MO) and a Spectronic 20D spectrophotometer (Milton Roy Company, Rochester, NY). Hematocrit (Hct) was measured in triplicate with a microhematocrit centrifuge (IEC, Model MB, Needham Heights, MA) and a Fisher Micro-capillary Tube Reader. Hematocrit measurements were not corrected for trapped plasma or for whole body hematocrit. Percent changes in PV, BV and red cell volume (RCV) during the tilt procedure were calculated from Hb and Hct measurements according to the formulas of Dill and Costill (1974):

$$\begin{aligned} \text{BV}_A &= \text{BV}_B (\text{Hb}_B/\text{Hb}_A) \\ \text{RCV}_A &= \text{BV}_A (\text{Hct}_A)/100 \\ \text{PV}_A &= \text{BV}_A - \text{CV}_A \\ \Delta\text{BV},\% &= 100 (\text{BV}_A - \text{BV}_B)/\text{BV}_B \\ \Delta\text{RCV},\% &= 100 (\text{CV}_A - \text{CV}_B)/\text{CV}_B \\ \Delta\text{PV},\% &= 100 (\text{PV}_A - \text{PV}_B)/\text{PV}_B \end{aligned}$$

where the subscripts B and A refer to measurements taken before and after the tilt procedure, respectively.

Hormone analyses. Vasopressin was extracted from 0.5 ml plasma samples by adsorption to bentonite and was eluted from the bentonite with a 4:1 (volume to volume) mixture of acetone and 1.0 N HCl. Average recovery was 80%; results were not corrected for recovery. Dried extracts were reconstituted to 0.25 ml with assay buffer (0.05 M phosphate buffer containing 0.01 M EDTA and 0.2% bovine serum albumin; pH = 7.4). Vasopressin was measured by radioimmunoassay (RIA) using a highly specific anti-AVP polyclonal antibody (raised in the laboratory of Dr. Charles Wood, University of Florida). ^{125}I -labeled AVP (DuPont, Wilmington, DE) was used as tracer, and AVP (Sigma) was used as standard. The range of the standard curve was from 0.05 to 10 pg per tube. The detection limit of the assay (90% of maximal binding) was 0.078 pg per tube, which translated to $0.39 \text{ pg} \cdot \text{ml}^{-1}$ after extraction of 0.5 ml of plasma. Values below $0.39 \text{ pg} \cdot \text{ml}^{-1}$ were assigned a value of $0.39 \text{ pg} \cdot \text{ml}^{-1}$ for statistical purposes. The intra-assay coefficient of variation for a low pool (0.40 pg per tube) was 4% ($\underline{n} = 10$) and for a high pool (4.0 pg per tube) was 14% ($\underline{n} = 10$). Interassay coefficient of variation was 7% (0.35 pg per tube; $\underline{n} = 13$) (Raff, Kane, & Wood, 1991).

For ACTH analysis, plasma samples and standard (0.5 ml) were extracted on powdered Corning glass (0.35mg per 0.5 ml of plasma, 100-200 mesh in double-distilled water, Corning Glass Works, Corning, NY) and eluted from the glass with a 1:1 (volume to volume) mixture of 0.25 N HCl and acetone. Dried extracts were reconstituted to 0.5 ml in assay buffer (0.5 M phosphate buffer, pH 7.4). Adrenocorticotrophic hormone was measured by RIA using an antibody specific to 1-39 hACTH raised in rabbits in the laboratories of Dr. Charles Wood and Dr. Maureen Keller-Wood (University of Florida). Standard (synthetic human 1-39 ACTH) was a gift of the National Hormone and Pituitary Program, NIDDK (University of Maryland School of

Medicine); ^{125}I -labeled ACTH was used as tracer. Values for extracted plasma samples were corrected for recovery using extracted standard. The lowest standard used in the assay was $20 \text{ pg} \cdot \text{ml}^{-1}$; values below this were assigned the value of $20 \text{ pg} \cdot \text{ml}^{-1}$ for statistical purposes. Interassay coefficients of variation were 19.2% and 9.8% from samples of mean concentrations of $33 \text{ pg} \cdot \text{ml}^{-1}$ ($n = 24$) and $76 \text{ pg} \cdot \text{ml}^{-1}$ ($n = 24$), respectively (Bell, Wood, & Keller-Wood, 1991).

Aldosterone was measured using a RIA kit from Diagnostic Products Corporation (Los Angeles, CA). Unextracted plasma samples were placed in ALDO antibody-coated tubes to which ^{125}I -ALDO was added; samples were then incubated for 3 hours at 37°C . The range of the standard curve was from 25 to $1200 \text{ pg} \cdot \text{ml}^{-1}$. Values below $25 \text{ pg} \cdot \text{ml}^{-1}$ were assigned the value of $25 \text{ pg} \cdot \text{ml}^{-1}$ for statistical purposes. Intraassay coefficients of variation (provided by Diagnostic Products) ranged from 2.7% for samples with a mean concentration of $803 \text{ pg} \cdot \text{ml}^{-1}$ to 8.3% for samples with a mean concentration of $52 \text{ pg} \cdot \text{ml}^{-1}$. Interassay coefficients of variation (provided by Diagnostic Products) ranged from 3.9% for samples with a mean concentration of $468 \text{ pg} \cdot \text{ml}^{-1}$ to 10.4% for samples with a mean concentration of $51 \text{ pg} \cdot \text{ml}^{-1}$.

Due to inadequate storage the plasma samples for PRA were damaged and the data is not presented.

Epinephrine (EPI) and norepinephrine (NE) were analyzed using high performance liquid chromatography (HPLC) using a Waters (Millipore Corporation, Milford, MA) HPLC system consisting of an injector unit (WISP TM Model 712B), pump (Model 510), and electrochemical detector (Model 460). The pH of 1 ml plasma samples was adjusted to 8.7 with 2 M Tris/EDTA buffer; 50 ml of internal standard (3,4, dihydroxybenzylamine; manufacturer-supplied) was then added. Norepinephrine, EPI and the standard were

extracted from this solution by adsorption onto alumina and were eluted from the alumina with a 2:1:1 (volume) mixture of glacial acetic acid, 10% sodium disulfide, and 5% EDTA. A 20 ml sample of extract was injected onto a reverse-phase C₁₈ column and EPI and NE were measured by electrochemical detection of the column effluent. Values were corrected for recovery using the internal standard. The intraassay coefficient of variation for NE was 1.4% while the interassay coefficient of variation was 3.8% (Convertino et al., 1991).

Total plasma PROT was determined using refractometry. This method is based on refraction and change in velocity of light waves as they cross an air/fluid interface. The higher the solute content, the greater the refraction (Raphael, 1976). Using this method, a 20 μ l drop of plasma was placed on the refractometer glass; light was admitted through a prism and PROT determination made to the nearest 0.2 g \cdot dl⁻¹. Both Na⁺ and K⁺ were determined to the nearest 0.1 mEq \cdot L⁻¹ from plasma samples using a Nova I ion-specific electrode system (Nova Biomedical, Waltham, MA).

Training

The 44 subjects who completed the initial testing were randomly assigned to one of two experimental (exercising) groups, or to a non-exercising control group. The experimental groups undertook endurance training on a treadmill (Trackmaster, Model TM 200E, JAS Mfg., Carrollton, TX) (TREAD; \underline{n} = 16), or endurance-plus-resistance (Nautilus™ plus MedX™) training (TREAD/RESIST; \underline{n} = 17). The remaining 11 subjects were assigned to the control (CONT) group. All subjects were asked not to change their lifestyle (e.g., diet and exercise habits) over the 6-month duration of the study.

Training for TREAD and TREAD/RESIST consisted of three sessions per week for 26 weeks. All training sessions began with 5 to 10 minutes of warm-up exercises and ended with a 5 minute cool-down walk. Initially all subjects exercised for 20 minutes at 40 to 50% of their maximal heart rate reserve (HRR_{max}) (Pollock & Wilmore, 1990). Exercise duration was increased by 5 minutes every 2 weeks until exercise time was 40 minutes. After the fifth week, exercise intensity was gradually increased to 60-70% HRR_{max} . Intensity was increased first by increasing the walking speed until the subject reached a comfortable, brisk pace; further increases in intensity were accomplished by raising the treadmill grade. Once subjects reached 40 minutes of exercise duration and 60-70% HRR_{max} , the intensity and duration were maintained through the 14th week. Rating of perceived exertion (RPE) during these sessions averaged approximately 12-13 initially (light/somewhat hard) and progressed to 13-14 (somewhat hard/hard, heavy). The average training intensity for weeks 1-13 was $62.6 \pm 4.2\%$ HRR_{max} . A $\dot{V}O_{2max}$ test was administered at T2 and training heart rates were adjusted for the latter half of the study based on the results of this test. Beginning in the 15th week, subjects gradually increased their intensity to 75-85% HRR_{max} while duration was increased to 45 minutes. The average training intensity and RPE for weeks 15-26 was $78.7 \pm 4.6\%$ HRR_{max} and 14-15 (hard), respectively.

The subjects in TREAD/RESIST additionally performed selected resistance training exercises during the 26 weeks of the study. One set each of 8-15 repetitions of biceps curl, triceps extension and leg press was performed 3 times per week, while one set of 8-12 repetitions of lumbar extensions was performed once a week. In the initial weeks of training, subjects were taught the proper lifting form and were required to exercise to moderate fatigue. After 13 weeks of training, subjects were encouraged to train at an intensity

that produced volitional muscle fatigue in 12-20 repetitions. When subjects could consistently complete 12-15 repetitions for the arm exercises, 15-20 repetitions for the leg exercise, or 10-15 repetitions for the lumbar extension exercise, resistance was increased by approximately 5%.

Based on a comparison to the T1 1-RM values, training intensity for the first 13 weeks averaged 67.9, 85.4, and 99.6% 1-RM for the leg press, biceps curl and triceps extension exercises, respectively. Intensity for the final 13 weeks averaged 73.7, 80.7, and 97.5% of the T2 1-RM for the leg press, biceps curl, and triceps extension, respectively. Training intensity for the lumbar extension averaged 61.5% of the T1 peak torque during weeks 1-13, and 66.4% of the T2 peak torque during weeks 14-26.

Data Analysis

Dependent Measures

The dependent measures consisted of the HR, SV, and BP measurements taken at successive time intervals during the tilt test. Calculated variables, such as mean arterial pressure ($MAP = DBP + 0.33 [SBP - DBP]$), TPR (MAP/\dot{Q}) and \dot{Q} were also dependent measures during the test.

Due to the assessment of several potential contributing mechanisms to any possible improvements in orthostatic response, other variables assumed dependent status in the various analyses. These variables included PV, total body and regional muscle mass, maximal strength, hormonal response to tilt, $\dot{V}O_{2max}$, and the response to cough.

Statistical Analyses

Forty-one of the original 44 subjects completed training and/or their obligations as control subjects. Of these 41, 8 were eliminated from statistical analyses due to β -blockade medication ($n = 3$), the presence of advanced cancer ($n = 1$), or pre-syncopal symptoms during T1 tilt testing ($n = 4$). Data from the subjects experiencing pre-syncopal symptoms during T1 tilt testing were analyzed separately. Therefore, the sample size used for all analyses, unless otherwise indicated, is 33.

Group characteristics, $\dot{V}O_2\text{max}$, strength, and body composition. In order to determine whether initial group characteristics were similar, the T1 age, height, weight, $\Sigma 7$, and relative $\dot{V}O_2\text{max}$ ($\text{ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) were each analyzed using a one-way analysis of variance (ANOVA) with Duncan's multiple range test. The change in $\Sigma 7$ and relative $\dot{V}O_2\text{max}$ values over 26 weeks was analyzed in a 2 X 3 (time X group) repeated measures ANOVA design.

A one-way ANOVA and a Duncan's multiple range post-hoc test performed on lower body lean mass measurement, and on the T1 maximum strength values for leg press (LP), biceps curl (BI), and triceps extension (TRI) values, and lumbar extension (LE) indicated that there were initial group differences that could be accounted for by including gender in the T1 ANOVA. Therefore, the analyses of the strength and lean mass changes were done in a 2 X 3 (time X group) analysis of covariance (ANCOVA) design using the T1 score as the covariate.

Cardiovascular responses. Means and standard deviations for HR, SV, \dot{Q} , SBP, DBP, MAP, and TPR were calculated. An inspection of the raw data

suggested that the multiple time measurements for each variable could be collapsed in order to provide a smaller number of representative values. Therefore a one-way repeated measures ANOVA using the four resting supine measurements was performed for each of the dependent measures. High *type I* error rates indicated that differences among the four values were due to random variation; the four values for each variable were therefore averaged to provide a single resting measurement.

Similarly, a series of repeated measures analyses for HR, SV, \dot{Q} , SBP, DBP, MAP, and TPR were performed on the measurements made during tilt (TILT) and supine recovery (REC). Separate analyses for HR, SV, and \dot{Q} were done on the measurements from minutes 2-5, 6-10 and 11-15 for both TILT and REC. Analyses of the BP variables and TPR were done on measurements from minutes 2-5 during both TILT and REC. An a priori decision was made not to include the raw data from TILT₀, TILT₁, REC₀, and REC₁ in these analyses since these time points represented transitional periods where values were rapidly changing.

The T1 resting values of HR, SV, \dot{Q} , SBP, DBP, MAP, and TPR were compared among the three groups using a one-way ANOVA. The effect of training on the resting variables was investigated in a 2 X 3 (test X group) repeated measures ANOVA.

Using the collapsed resting, tilt and recovery values, a 2 X 3 X 11 (test X group X time) repeated measures ANOVA was used to compare rest, tilt and recovery values for each dependent variable. A significant *test* effect for a particular variable was further evaluated by creating a mean value (collapsed over time and group) for each test. A significant *test X group* interaction was further analyzed in a 2 X 3 (test X group) repeated measures ANOVA using the mean value for a particular variable (collapsed over time) for each group

and test. A significant *time* effect for a particular variable was evaluated by comparing the TILT and REC values, collapsed over group and test, to the resting value in a one-way ANOVA with 11 levels of time.

Plasma volume and hormone/electrolyte responses. Plasma volume measurements were obtained successfully at both T1 and T3 in only 18 of 33 subjects. Because of the small number of subjects with duplicate PV measurements in each of the training groups, subjects in TREAD and TREAD/RESIST were combined into a single group (TRAIN) for PV statistical analyses. In order to determine whether initial group values were similar, the T1 pretilt PV, BV, RCV, Hb, and Hct were each analyzed using a one-way ANOVA with Duncan's multiple range post-hoc test. To determine whether tilt and/or training affected these variables, PV, BV, RCV, Hb, and Hct were each analyzed in a 2 X 4 (group X time) repeated measures ANOVA design. The time levels represented *pretilt* and *tilt* at both T1 and T3. The percent change in PV, BV, and RCV during tilt at T1 and T3 were analyzed in a 2 X 2 (group X time) repeated measures ANOVA. Because of the necessity of combining TREAD and TREAD/RESIST into a single group for the various BV analyses, the hormonal responses were similarly analyzed in 2 X 4 (group X time) repeated measures ANOVA designs. The time levels represented *pretilt* and *tilt* at both T1 and T3.

Cough test. The parameters measured during the cough test represented the reflex responses in the presumed baroreceptor-mediated event; no direct measure of the reflex stimulus (e.g., intra-arterial pressure measurements) was available. The resting R-R interval for each cough test was calculated as the mean of five intervals occurring prior to the onset of coughing. In the minute following the cessation of coughing, the following parameters were identified: the minimum R-R interval, the time (in seconds)

after cough cessation at which the minimum R-R interval occurred, and the number of R-R intervals occurring between the cessation of coughing and the minimum R-R. From these parameters, the difference between the resting and minimum R-R was calculated (Δ R-R). Means and standard deviations of the first 40 intervals after the cough were calculated and transformed to HR values with the formula: $HR = 60/R-R$.

To determine whether values from the three supine and three tilt cough trials were comparable, the resting R-R, minimum R-R, Δ R-R, time of minimum R-R, and interval of minimum R-R were each analyzed in a one-way repeated measures ANOVA. Based on the results of these tests, the three supine and three tilt values were each averaged. Using the averaged values, group differences at T1 were assessed using a one-way ANOVA and Duncan's multiple range test. The effect of training was analyzed with an ANCOVA design with the T1 values as the covariate.

Analysis of the 40 beats after the cessation of coughing was done on HR values averaged every five beats. A one-way ANOVA with nine levels of time was used to compare the resting HR with the eight averaged post-cough HRs for each test and group. To assess the effect of tilt and training, a 4 X 3 (test X group) repeated measures ANOVA was performed for each of the nine time points. The four tests were T1 supine, T1 tilt, T3 supine and T3 tilt.

In all cases, statistical probabilities are presented as the chances of concluding wrongly that the mean values obtained during the tilt test were due to true differences and did not arise from random variability given the sample size of this experiment. A $p \leq 0.05$ was required for statistical significance.

CHAPTER 4 RESULTS

Subject Characteristics

Descriptive data on age, height, weight, and sum of seven skinfolds ($\Sigma 7$) at the start of training are presented for the control (CONT), treadmill (TREAD), and treadmill plus resistance (TREAD/RESIST) groups in Table 4-1. The results of the ANOVA performed to assess differences in initial subject characteristics indicated a large *type I* error rate for weight ($p = 0.15$), height ($p = 0.14$) and $\Sigma 7$ ($p = 0.49$). Thus, any differences in these three variables at the start of the training program were due to random variation. However, the probability of a *type I* error for the age analysis was small ($p = 0.01$). Post hoc analysis using Duncan's multiple range test indicated that TREAD was older than CONT at the start of the program.

Table 4-1. Characteristics of Control, Treadmill, and Treadmill/Resistance Training Groups at the Start of 6 Months of Exercise Training.

Group	Age (yrs)	Height (cm)	Weight (kg)	$\Sigma 7$ (mm)
CONT ($\underline{n} = 9$)	65.8 \pm 6.7	164.9 \pm 8.5	71.0 \pm 12.7	186 \pm 54
TREAD ($\underline{n} = 14$)	72.4 \pm 4.5*	161.4 \pm 6.6	61.8 \pm 14.2	173 \pm 57
TREAD/RESIST ($\underline{n} = 10$)	68.7 \pm 3.8	168.8 \pm 11.4	73.4 \pm 17.8	150 \pm 73

Values are mean \pm S.D.

CONT = Control; TREAD = Treadmill; TREAD/RESIST = Treadmill/Resistance; $\Sigma 7$ = Sum of 7 skinfolds (triceps, chest, subscapula, axilla, abdomen, suprailium, thigh)

* $p \leq 0.01$, greater than CONT

Training Responses

Maximal Oxygen Uptake

The T1 and T3 $\dot{V}O_{2\max}$ ($\text{ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) values for CONT, TREAD, and TREAD/RESIST are listed in Table 4-2. The results of the ANOVA to assess differences in T1 values indicated that any differences among groups in initial $\dot{V}O_{2\max}$ were due to random variation ($p = 0.32$). The 2 X 3 (test X group) repeated measures analysis used to assess the effects of training resulted in a *type I* error rate of < 0.01 for detecting a *test X group* interaction. Follow up analyses showed that after 26 weeks of training, TREAD and TREAD/RESIST increased $\dot{V}O_{2\max}$ by 16.4% and 13.7%, respectively ($p \leq 0.01$). The 5.3% decline in the $\dot{V}O_{2\max}$ of CONT during the 26 week study period could be ascribed to random variation ($p = 0.11$).

Table 4-2. $\dot{V}O_{2\max}$ ($\text{ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) Responses of Control, Treadmill, and Treadmill/Resistance Groups Before (T1) and After (T3) 6 Months of Exercise Training.

Group	<u>n</u>	T1	T3
CONT	9	22.8 ± 3.7	21.6 ± 4.1
TREAD	14	22.0 ± 4.4	$25.6 \pm 5.6^*$
TREAD/RESIST	10	24.8 ± 5.0	$28.2 \pm 5.4^*$

Values are mean \pm S.D.

CONT = Control; TREAD = Treadmill; TREAD/RESIST = Treadmill/Resistance

* $p \leq 0.01$, greater than corresponding T1 value

Strength

In strength testing, there were 10 subjects who did not complete T3 leg press (LP) testing. Seven subjects had sustained back or knee injuries over the 6 month interval which precluded LP testing and/or training; three subjects did not complete their strength testing obligations at T3. Four subjects did not complete T3 biceps curl (BI) and triceps extension (TRI) testing; two of these subjects had sustained injuries which precluded testing and/or training, while the other two subjects did not complete their T3 testing obligations. Therefore, the sample size for LP 1-RM strength testing was 23, while for BI and TRI testing it was 29. The sample size for lumbar extension (LE) testing was 19.

The T1 and T3 values for LP, BI, TRI, and LE strength are listed in Table 4-3. The results of the ANOVA used to assess differences in T1 values indicated a low probability of a *type I* error in the detection of group differences for LP ($p < 0.01$), BI ($p < 0.01$), TRI ($p = 0.05$) and LE ($p = 0.03$). The results of Duncan's post hoc test indicated that TREAD/RESIST had higher strength scores than TREAD in LP, BI, and TRI and had higher scores than both TREAD and CONT in LE. However, when gender was used as a covariate in the T1 analysis, the resulting high p-values ($p = 0.71, 0.74, 0.58, 0.67$ for LP, BI, TRI, and LE respectively) indicated that once gender was accounted for, any differences among groups were due to random variation.

The effect of training on all strength measures was therefore analyzed with an analysis of covariance (ANCOVA) design using the T1 strength scores as the covariate. Table 4-3 lists the T3 group means adjusted for the T1 scores. ANCOVA results indicated that differences in adjusted T3 LP scores could be

accounted for by random variation ($p = 0.55$). Thus, strength training by TREAD/RESIST did not improve leg/buttocks strength to a greater extent than the changes seen in TREAD and CONT. Using absolute strength scores, TREAD/RESIST increased strength in LP by 16.5% after 26 weeks of training. However, TREAD and CONT also increased LP strength by 18.9% and 8.2%, respectively.

Table 4-3. Strength Testing Scores of Control, Treadmill, and Treadmill/Resistance Groups Before (T1) and After (T3) 6 Months of Exercise Training.

Variable	Group	<u>n</u>	T1	T3	Adjusted T3 [§]
LP (lbs)	CONT	5	114.0 ± 49.9	123.3 ± 37.6	154.6 ± 10.8
	TREAD	11	108.1 ± 63.2	128.5 ± 75.4	166.7 ± 6.9
	TREAD/RESIST	7	216.3 ± 127.5**	251.9 ± 149.8	170.0 ± 9.5
BI (lbs)	CONT	6	47.1 ± 22.7	46.3 ± 21.5	43.8 ± 2.3
	TREAD	14	35.9 ± 14.1	36.6 ± 16.1	46.5 ± 1.6
	TREAD/RESIST	9	57.2 ± 22.8**	71.9 ± 32.5	58.2 ± 2.0 [†]
TRI (lbs)	CONT	6	36.7 ± 16.9	35.8 ± 16.6	33.4 ± 2.5
	TREAD	14	28.2 ± 8.9	29.3 ± 10.1	36.7 ± 1.6
	TREAD/RESIST	9	43.1 ± 17.3**	55.8 ± 24.1	46.0 ± 1.9 [†]
LE (Nm) ^a	CONT	6	145.1 ± 39.8	149.4 ± 33.9	190.6 ± 12.8
	TREAD	7	142.4 ± 52.8	147.8 ± 71.9	191.9 ± 11.9
	TREAD/RESIST	6	269.9 ± 156.3*	274.8 ± 170.8	182.1 ± 14.2

T1 and T3 values are mean ± S.D.; Adjusted T3 values are mean ± S.E.

CONT = Control; TREAD = Treadmill; TREAD/RESIST = Treadmill/Resistance; LP = Leg press; BI = Biceps curl; TRI = Triceps extension; LE = Lumbar extension

[§] Adjusted for T1 strength scores

* $p \leq 0.05$, greater than TREAD and CONT at T1

** $p \leq 0.05$, greater than TREAD at T1

[†] adjusted T3 score greater than CONT and TREAD

^a Newton-meters, averaged over the number of angles tested

Analysis of covariance results indicated that the adjusted T3 BI scores of TREAD/RESIST were greater than those of either TREAD ($p < 0.01$) or CONT ($p < 0.01$). The adjusted TRI scores for TREAD/RESIST were also greater than those for both TREAD ($p < 0.01$) and CONT ($p < 0.01$). Using absolute strength scores, TREAD/RESIST increased strength in BI and TRI by 25.7% and 29.5%, respectively, while both TREAD and CONT showed changes of less than 5% in these exercises.

Analysis of covariance results for LE strength indicated that differences among groups in adjusted T3 LE scores could be accounted for by random variation ($p = 0.88$). Thus, lumbar extension training by TREAD/RESIST did not improve lower back strength to a greater extent than the changes seen in TREAD and CONT. Using absolute strength scores, TREAD/RESIST increased strength in LE by 1.8% after 26 weeks of training. However, TREAD and CONT also increased LE strength by 3.8% and 3.0%, respectively.

Body Composition

Two control subjects did not complete testing obligations at T3; therefore, calculation of muscle mass data was based on a sample size of 32, while sum of seven skinfold ($\Sigma 7$) and girth data were based on a sample size of 31. Means and standard deviations for CONT, TREAD, and TREAD/RESIST for body weight, $\Sigma 7$, arm and leg girths, and lean mass measures are listed in Table 4-4. The results of the ANOVA used to assess group differences in T1 values indicated a low probability of a *type I* error for lower body lean mass ($p = 0.04$) and for arm lean mass ($p = 0.04$). The results of Duncan's post hoc test indicated that TREAD/RESIST had greater arm and lower body lean mass than TREAD. The probability levels for *type I* errors in detecting group differences at T1 for arm girth, leg girth, $\Sigma 7$, body

Table 4-4. Body Composition Measurements for Control, Treadmill, and Treadmill/Resistance Groups Before (T1) and After (T3) 6 Months of Exercise Training.

	T1	T3	Adjusted T3*
CONT			
Σ7 (mm) (<u>n</u> = 7)	186 ± 54	191 ± 62	---
Body weight (kg) (<u>n</u> = 11)	71.0 ± 12.7	72.4 ± 14.2	---
Arm girth (cm) (<u>n</u> = 7)	31.0 ± 4.0	31.9 ± 3.6	---
Leg girth (cm) (<u>n</u> = 7)	54.8 ± 5.5	54.9 ± 5.0	---
Arm lean mass (kg) (n=8)	3.8 ± 1.3	3.9 ± 1.3	4.0 ± 1.2
Trunk lean mass (kg) (n=8)	18.9 ± 4.5	19.2 ± 5.2	20.4 ± 0.5
Total body lean mass (kg) (<u>n</u> = 8)	40.7 ± 10.7	41.3 ± 10.6	41.7 ± 0.3
Lower body lean mass (kg) (<u>n</u> = 8)	14.0 ± 3.5	14.6 ± 3.4	14.7 ± 0.2
TREAD (<u>n</u> = 14)			
Σ7 (mm)	173 ± 57	159 ± 58§	---
Body weight (kg)	61.8 ± 14.2	60.8 ± 14.6§	---
Arm girth (cm)	28.8 ± 3.7	28.5 ± 3.7	---
Leg girth (cm)	49.7 ± 4.0	48.3 ± 3.9	---
Arm lean mass (kg)	3.2 ± 1.3	3.4 ± 1.3	4.1 ± 0.9
Trunk lean mass (kg)	18.9 ± 4.7	18.7 ± 4.4	20.0 ± 0.3
Total body lean mass (kg)	37.0 ± 8.5	37.1 ± 8.5	41.0 ± 0.3
Lower body lean mass (kg)	12.5 ± 2.7	12.7 ± 2.8	14.3 ± 0.2
TREAD/RESIST (<u>n</u> = 10)			
Σ7 (mm)	150 ± 73	146 ± 67	---
Body weight (kg)	73.4 ± 17.8	73.7 ± 17.9	---
Arm girth (cm)	31.5 ± 5.0	32.2 ± 4.5§	---
Leg girth (cm)	52.7 ± 5.4	51.5 ± 5.4	---
Arm lean mass (kg)	4.9 ± 2.1	5.1 ± 1.9	4.1 ± 1.1
Trunk lean mass (kg)	23.0 ± 6.7	22.5 ± 6.4	19.8 ± 0.4
Total body lean mass (kg)	47.1 ± 13.8	46.8 ± 13.1	41.0 ± 0.3
Lower body lean mass (kg)	16.4 ± 4.5†	16.7 ± 4.3	14.4 ± 0.2

T1 and T3 values are mean ± S.D.; adjusted T3 values are mean ± S.E.

CONT = Control; TREAD = Treadmill; TREAD/RESIST =

Treadmill/Resistance; Σ7 = Sum of seven skinfolds (triceps, chest, subscapula, axilla, abdomen, suprailium, thigh)

* Adjusted for T1 lean mass values

† $p \leq 0.05$, TREAD/RESIST > TREAD at T1

§ Change from the respective T1 value

weight, total body lean mass, and trunk lean mass were 0.07, 0.27, 0.49, 0.15, 0.10, 0.49 respectively.

When gender was used as a covariate in the T1 analyses for arm and lower body lean mass, the resulting high p-values ($p = 0.35$ and 0.52 , respectively) indicated that, once gender was accounted for, any initial differences among groups were due to random variation. The effect of training on all lean mass measures was therefore analyzed with an ANCOVA design using the T1 measure as the covariate. The results indicated that the changes with training for total body lean mass, lower body lean mass, arm lean mass, and trunk lean mass could be ascribed to random variation ($p = 0.27, 0.32, 0.75$, and 0.64 , respectively).

Analyses of the effect of training on $\Sigma 7$, body weight, arm girth and leg girth were each done in a 2×3 (time \times group) repeated measures ANOVA. The *type I* error rates for detecting a *time \times group* interaction for $\Sigma 7$, body weight, arm girth, and leg girth were 0.03, 0.05, 0.01, and 0.37 respectively. Follow up analyses indicated that there was a decrease in the $\Sigma 7$ ($p = 0.01$) and body weight ($p = 0.02$) for TREAD. Differences in $\Sigma 7$ and body weight between T1 and T3 for CONT ($p = 0.41$ and 0.23 , respectively) and TREAD/RESIST ($p = 0.32$ 0.62 , respectively) were due to random variation. The follow up analysis for arm girth indicated that TREAD/RESIST had an increase in arm girth ($p = 0.03$), while changes in arm girth for TREAD and CONT from T1 to T3 were due to random variation ($p = 0.16$ and 0.10 , respectively).

Cardiovascular Responses to Tilt

Analyses to Average Data

Means and standard deviations for the overall (averaged over tests and groups) heart rate (HR), stroke volume (SV), cardiac output (\dot{Q}), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and total peripheral resistance (TPR) responses to tilt were calculated for minutes 15, 20, 25, and 30 of rest, minutes 0 through 15 of tilt (TILT) and minutes 0 through 15 of recovery (REC) (Table 4-5). Inspection of these data suggested that the multiple time measurements for each variable could be averaged in order to provide a smaller number of representative values. A repeated measures ANOVA using the four resting supine measurements (i.e., minutes 15, 20, 25, and 30) showed that differences among the four time points for SV, \dot{Q} , SBP, DBP, MAP, and TPR were due to random variation (Table 4-6). Therefore, the four values for each variable were averaged to provide a single resting measurement. The results of the test for HR indicated a low probability of a *type I* error ($p = 0.05$). Although this suggests that differences among the four resting HR measurements were due to some factor associated with *time*, inspection of the raw data (Table 4-5) shows that the four HR values ranged from 63.0 to 64.1 $\text{b} \cdot \text{min}^{-1}$. Since this difference is not physiologically meaningful, the four resting HR values were also averaged to provide a single resting value.

Similar repeated measures analyses were performed on the measurements from minutes 2-5, 6-10 and 11-15 for HR, SV, and \dot{Q} for both

Table 4-5. Overall Heart Rate, Stroke Volume, Cardiac Output, Blood Pressure and Peripheral Resistance Response to Tilt, Averaged Over Groups and Tests.

Time	HR (b•min ⁻¹)	SV (ml)	Q̇ (L•min ⁻¹)	SBP (mmHg)	DBP (mmHg)	MAP (mmHg)	TPR *
Rest (min)							
15	64.1± 9.4	50.9±10.8	3.24±0.76	126.4±15.2	77.0±6.3	93.3±7.9	2483±597
20	63.2± 9.2	52.2±11.4	3.26±0.76	125.4±14.3	76.6±6.7	92.7±7.9	2469±704
25	63.0± 9.3	52.1±11.6	3.26±0.80	126.8±13.9	77.0±6.4	93.4±7.8	2507±677
30	63.5± 8.9	51.8±11.2	3.26±0.75	127.7±15.2	77.6±6.5	94.1±8.2	2454±616
Tilt (min)							
0	68.9±12.1	38.6± 8.5	2.61±0.54	124.1±16.2	80.5±8.9	94.9±9.9	3052±761
1	71.2±10.6	37.0± 7.5	2.61±0.51	124.9±16.5	81.2±9.2	95.6±10.4	3041±718
2	71.4±10.3	36.6± 7.3	2.58±0.50	127.1±16.1	81.8±7.7	96.7±9.2	3096±701
3	70.7± 9.7	36.8± 7.8	2.57±0.52	127.6±16.3	82.1±7.4	97.1±9.0	3144±663
4	70.4±10.1	37.2± 8.2	2.59±0.53	126.7±13.7	82.4±8.3	97.0±9.0	3127±650
5	70.7±10.6	37.0± 8.0	2.58±0.52	128.2±15.4	82.3±8.1	97.5±8.8	3160±714
6	71.2±10.5	37.0± 7.8	2.60±0.50	---	---	---	---
7	71.4±10.4	37.0± 8.0	2.61±0.50	---	---	---	---
8	71.8±10.8	37.3± 8.2	2.65±0.48	---	---	---	---
9	72.1±10.8	37.4± 8.5	2.66±0.55	---	---	---	---
10	72.0±11.5	37.4± 8.9	2.65±0.51	128.6±16.8	82.2±8.3	97.5±9.4	3015±622
11	72.7±11.4	37.6± 8.4	2.67±0.48	---	---	---	---
12	73.5±11.4	36.7± 8.0	2.65±0.48	---	---	---	---
13	73.2±11.7	37.4± 9.0	2.68±0.54	---	---	---	---
14	73.8±12.1	37.2± 9.1	2.69±0.49	---	---	---	---
15	74.1±12.9	36.9± 9.3	2.66±0.47	126.2±17.1	81.5±8.2	96.2±9.9	2913±599
Recovery (min)							
0	67.5±11.1	51.1±12.4	3.40±0.81	128.2±15.5	77.5±6.9	94.1±8.9	2413±689
1	64.2±10.5	52.1±12.0	3.29±0.71	128.6±14.1	78.3±6.9	94.9±7.9	2445±603
2	62.9±10.5	50.4±12.4	3.12±0.67	128.4±15.2	78.6±6.8	95.1±8.5	2589±690
3	62.6±10.2	50.2±12.8	3.07±0.68	128.3±14.3	78.6±6.9	95.1±8.1	2707±705
4	62.3±10.0	49.2±11.4	3.00±0.65	128.5±14.8	79.1±7.3	95.4±8.6	2725±689
5	62.5±10.2	48.7±11.6	2.99±0.66	128.4±14.6	78.7±7.4	95.1±8.7	2733±684
6	62.2± 9.9	48.8±11.9	2.97±0.66	---	---	---	---
7	62.5± 9.7	48.3±11.9	2.97±0.69	---	---	---	---
8	62.3± 9.7	47.8±11.9	2.93±0.69	---	---	---	---
9	62.0± 9.2	48.2±11.2	2.94±0.66	---	---	---	---
10	62.1± 9.3	48.0±11.4	2.94±0.69	127.5±16.2	78.3±6.5	94.5±8.3	2751±858

Table 4-5--continued.

Time	HR (b•min ⁻¹)	SV (ml)	\dot{Q} (L•min ⁻¹)	SBP (mmHg)	DBP (mmHg)	MAP (mmHg)	TPR *
Recovery (min)							
11	62.5± 9.3	48.2±12.3	2.96±0.72	---	---	---	---
12	62.5± 8.9	47.9±11.5	2.96±0.69	---	---	---	---
13	62.5± 9.6	47.7±12.2	2.93±0.70	---	---	---	---
14	62.4± 8.7	48.4±12.1	2.97±0.69	---	---	---	---
15	62.0± 8.6	47.5±11.9	2.93±0.69	126.8±15.1	78.6±7.2	94.5±8.6	2758±816

* dyne sec•cm⁻⁵

Values are mean ± S.D.; HR = Heart rate; SV = Stroke volume, \dot{Q} = Cardiac output, SBP = Systolic blood pressure; DBP = Diastolic blood pressure; MAP = Mean arterial pressure; TPR = Total peripheral resistance.

tilt (TILT) and recovery (REC). Analyses of SBP, DBP, MAP, and TPR were done on measurements from minutes 2-5 for both TILT and REC. An a priori decision was made not to include the raw data from TILT₀, TILT₁, REC₀ and REC₁ in these analyses since these time points represent periods of transition.

The probability of a *type I* error in detecting a *time* effect in each of these analyses is presented in Table 4-6. Where the probability levels were high, it was concluded that any differences among the measurements were due to random variation, and that the measurements could be averaged to provide a single representative value. However, several of the analyses produced low probability levels, leading to an initial conclusion that the differences were due to some factor associated with *time*. In these cases, inspection of the raw data presented in one minute intervals (Table 4-5) showed that these differences were physiologically small. For example, the range of HR values at TILT₆₋₁₀ was from 71.2 to 72.1 b•min⁻¹ (range = 0.9 b•min⁻¹). Similarly, the ranges for the HR values at TILT₁₁₋₁₅ and REC₆₋₁₀

Table 4-6. Analyses to Average Data: *Type I* Error Rates for Detecting a Time Effect Within Each Time Period for Heart Rate, Stroke Volume, Cardiac Output, Blood Pressure, and Total Peripheral Resistance.

	HR	SV	\dot{Q}	SBP	DBP	MAP	TPR
Rest	0.05	0.58	0.91	0.13	0.61	0.22	0.73
TILT 2-5	0.28	0.13	0.55	0.78	0.74	0.52	0.26
TILT 6-10	0.02	0.11	0.66	---	---	---	---
TILT 11-15	<0.01	0.03	0.85	---	---	---	---
REC 2-5	0.30	0.01	0.01	0.91	0.71	0.91	0.01
REC 6-10	<0.01	<0.01	<0.01	---	---	---	---
REC 11-15	0.71	0.45	0.67	---	---	---	---

HR = Heart rate; SV = Stroke volume, \dot{Q} = Cardiac output, SBP = Systolic blood pressure; DBP = Diastolic blood pressure; MAP = Mean arterial pressure; TPR = Total peripheral resistance; REC = Recovery

were 1.4 and 0.3 $\text{b} \cdot \text{min}^{-1}$, respectively. For the values of SV at TILT₁₁₋₁₅, REC₂₋₅, and REC₆₋₁₀, the ranges were 0.9, 1.7, and 1.0 ml, respectively. The ranges for the values at REC₂₋₅ and REC₆₋₁₀ were 0.13 and 0.04 $\text{L} \cdot \text{min}^{-1}$, respectively. Finally, the range of values for TPR during REC₂₋₅ was 194 $\text{dyne sec} \cdot \text{cm}^{-5}$. Therefore, because of the small differences among the values during each of the pre-determined time periods, the raw data within each time period were averaged. These data are presented in Tables 4-7--4-10.

Effect of Training on Resting Variables

Resting values of HR, SV, \dot{Q} , SBP, DBP, MAP, and TPR at T1 and T3 are shown in Table 4-11. The probability levels for a *type I* error in detecting a group difference in resting measurements at T1 (HR, $p = 0.14$; SV, $p = 0.40$; \dot{Q} , $p = 0.96$; SBP, $p = 0.58$; DBP, $p = 0.63$; MAP, $p = 0.55$; TPR, $p = 0.99$) indicate that

Table 4-7. Averaged Heart Rate and Stroke Volume Responses to 70° Head-up Tilt for Control, Treadmill, and Treadmill/Resistance Groups Before (T1) and After (T3) 6 Months of Exercise Training.

Time	Control (<u>n</u> = 9)		Treadmill (<u>n</u> = 14)		Treadmill/Resistance (<u>n</u> = 10)	
	T1	T3	T1	T3	T1	T3
Heart Rate (b•min ⁻¹)						
Rest	61.6± 6.0	61.0±5.2	68.5±10.0	64.8± 9.5	61.7±10.7	60.4±10.6
Tilt						
0	66.6±11.5	66.4±7.7	74.0±15.4	70.6±12.6	66.4±12.8	65.5±13.3
1	67.8± 7.8	69.2±7.4	75.9±12.7	71.7±11.5	68.8±11.3	68.1±12.0
2-5	67.6± 7.7	68.1±5.6	74.3±11.8	71.8±11.0	70.3±11.3	67.4±11.6
6-10	67.9± 8.2	69.3±5.3	75.6±12.1	73.3±12.2	71.1±12.9	68.5±12.6
11-15	69.2± 9.2	70.3±6.8	78.5±12.9	75.1±13.1	72.4±13.2	69.9±13.1
Recovery						
0	62.1± 5.9	64.4±3.4	73.8±15.3	69.4±11.8	67.7±12.3	64.0±13.2
1	60.0± 5.6	60.3±5.5	70.4±14.5	66.8±10.7	63.6±10.7	60.1± 9.7
2-5	59.0± 4.7	58.0±4.8	68.3±13.5	64.2±10.5	61.6±10.0	58.9± 9.6
6-10	59.0± 5.3	58.7±5.4	67.6±12.4	62.2± 8.9	62.0± 9.9	58.7±10.1
11-15	59.8± 4.8	59.9±4.9	67.2±11.6	62.4± 7.9	62.0±10.1	58.5±10.5
Stroke Volume (ml)						
Rest	50.1±10.4	51.2±12.2	45.7±7.3	55.1±10.4	50.9±13.0	47.3±10.3
Tilt						
0	36.1±12.2	37.1± 9.0	34.2±5.9	38.5± 8.7	43.6± 7.0	41.0± 8.9
1	36.4± 9.2	35.2± 7.4	33.7±5.6	37.5± 6.3	40.4± 9.3	39.1± 8.8
2-5	34.7± 8.0	35.5± 6.4	33.9±5.4	36.9± 6.8	39.6± 9.7	39.0± 8.4
6-10	35.5± 8.3	36.2± 7.3	33.5±4.7	36.8± 6.6	41.1±11.9	38.4± 8.5
11-15	36.0± 8.6	36.7± 8.1	33.2±5.7	37.9± 6.9	40.7±12.6	39.3±10.1
Recovery						
0	50.3± 8.7	52.4±12.5	44.0±7.0	54.0±12.0	51.7±17.3	46.7±11.1
1	50.5±10.1	53.5±14.0	45.0±8.0	54.3±10.1	55.6±16.4	48.8±11.6
2-5	47.8± 8.9	52.4±13.1	44.0±7.0	51.8±11.4	49.9±16.3	45.4±11.8
6-10	46.8±10.4	48.8±13.8	43.0±5.8	51.4± 9.5	48.8±16.4	44.1±12.8
11-15	44.9± 9.3	49.5±14.2	42.4±6.0	51.9±11.5	47.8±16.8	45.3±13.1

Values are mean ± S.D.

Table 4-8. Averaged Cardiac Output Responses to 70° Head-up Tilt for Control, Treadmill, and Treadmill/Resistance Groups Before (T1) and After (T3) 6 Months of Exercise Training.

Time	Control (<u>n</u> = 9)		Treadmill (<u>n</u> = 14)		Treadmill/Resistance (<u>n</u> = 10)	
	T1	T3	T1	T3	T1	T3
Cardiac Output (L•min ⁻¹)						
Rest	3.05±0.57	3.09±0.65	3.13±0.69	3.55±0.88	3.08±0.69	2.80±0.53
Tilt						
0	2.30±0.52	2.41±0.42	2.50±0.58	2.70±0.67	2.79±0.29	2.61±0.36
1	2.54±0.59	2.39±0.36	2.56±0.60	2.70±0.50	2.72±0.54	2.62±0.44
2-5	2.32±0.43	2.40±0.32	2.51±0.52	2.62±0.51	2.71±0.49	2.59±0.47
6-10	2.36±0.45	2.49±0.39	2.53±0.45	2.66±0.46	2.81±0.53	2.63±0.48
11-15	2.44±0.44	2.55±0.42	2.57±0.43	2.79±0.46	2.83±0.48	2.65±0.47
Recovery						
0	3.12±0.52	3.35±0.75	3.21±0.67	3.69±0.90	3.39±0.95	2.88±0.61
1	3.00±0.51	3.15±0.70	3.05±0.67	3.65±0.74	3.46±0.86	2.86±0.34
2-5	2.81±0.48	3.00±0.64	2.97±0.59	3.27±0.65	2.96±0.76	2.60±0.28
6-10	2.74±0.54	2.81±0.66	2.89±0.59	3.17±0.75	2.91±0.75	2.49±0.40
11-15	2.67±0.51	2.92±0.72	2.84±0.62	3.20±0.82	2.86±0.79	2.61±0.44

Values are mean ± S.D.

any differences among groups at the start of the program were due to random variation. In a 2 X 3 (test X group) ANOVA to analyze the effect of training on resting HR, the magnitude of the *p*-value for the *test X group* interaction (*p* = 0.30) suggests that group assignment did not affect resting HR over the 6 month interval. However, *p*-value for the *test* effect for resting HR was low (*p* = 0.04), suggesting a systematic difference between the T1 and T3 measurements. A comparison of the resting means combined over all groups indicated that the T3 resting HR ($62.4 \pm 8.9 \text{ b} \cdot \text{min}^{-1}$) was $2.1 \text{ b} \cdot \text{min}^{-1}$ (3.3%) lower than the T1 resting HR ($64.5 \pm 9.7 \text{ b} \cdot \text{min}^{-1}$) (*p* = 0.02).

Table 4-9. Averaged Systolic and Diastolic Blood Pressure Responses to 70° Head-up Tilt for Control, Treadmill, and Treadmill/Resistance Groups Before (T1) and After (T3) 6 Months of Exercise Training.

Time	Control (<u>n</u> = 9)		Treadmill (<u>n</u> = 14)		Treadmill/Resistance (<u>n</u> = 10)	
	T1	T3	T1	T3	T1	T3
Systolic Blood Pressure (mmHg)						
Rest	124 ± 9	122 ± 11	127 ± 12	135 ± 20	122 ± 9	126 ± 17
Tilt						
0	120 ± 14	123 ± 15	124 ± 13	128 ± 20	123 ± 14	126 ± 22
1	120 ± 13	126 ± 15	125 ± 14	125 ± 19	125 ± 12	129 ± 27
2-5	126 ± 12	127 ± 13	126 ± 13	130 ± 16	125 ± 13	133 ± 24
6-10	127 ± 15	127 ± 13	125 ± 13	134 ± 22	126 ± 11	131 ± 22
11-15	126 ± 16	125 ± 12	123 ± 12	129 ± 23	124 ± 17	132 ± 22
Recovery						
0	124 ± 15	127 ± 15	127 ± 18	135 ± 17	122 ± 12	131 ± 14
1	126 ± 12	131 ± 11	127 ± 14	135 ± 16	121 ± 11	130 ± 17
2-5	126 ± 12	131 ± 11	126 ± 14	133 ± 17	123 ± 12	132 ± 18
6-10	126 ± 13	128 ± 12	124 ± 12	132 ± 19	125 ± 12	130 ± 26
11-15	127 ± 13	130 ± 13	123 ± 12	129 ± 18	124 ± 12	131 ± 22
Diastolic Blood Pressure (mmHg)						
Rest	77 ± 8	78 ± 7	79 ± 4	75 ± 7	77 ± 6	78 ± 4
Tilt						
0	83 ± 9	79 ± 11	79 ± 4	80 ± 9	82 ± 8	82 ± 14
1	83 ± 12	80 ± 10	79 ± 5	81 ± 8	83 ± 8	81 ± 13
2-5	83 ± 11	82 ± 9	81 ± 3	80 ± 8	84 ± 8	84 ± 8
6-10	83 ± 9	82 ± 9	83 ± 4	79 ± 8	85 ± 10	83 ± 10
11-15	81 ± 12	83 ± 9	81 ± 4	81 ± 9	81 ± 9	82 ± 8
Recovery						
0	76 ± 9	77 ± 8	78 ± 6	77 ± 7	79 ± 8	78 ± 6
1	79 ± 10	80 ± 8	80 ± 5	77 ± 6	79 ± 8	78 ± 6
2-5	79 ± 11	79 ± 8	79 ± 5	77 ± 6	80 ± 7	80 ± 5
6-10	77 ± 10	79 ± 8	78 ± 4	75 ± 5	81 ± 7	81 ± 5
11-15	78 ± 12	79 ± 9	78 ± 5	76 ± 5	81 ± 7	80 ± 5

Values are mean ± S.D.

Table 4-10. Averaged Mean Arterial Blood Pressures and Total Peripheral Resistance Responses to 70° Head-up Tilt for Control, Treadmill, and Treadmill/Resistance Groups Before (T1) and After (T3) 6 Months of Exercise Training.

Time	Control (<u>n</u> = 9)		Treadmill (<u>n</u> = 14)		Treadmill/Resistance (<u>n</u> = 10)	
	T1	T3	T1	T3	T1	T3
Mean Arterial Pressure (mmHg)						
Rest	92 ± 8	92 ± 8	95 ± 6	95 ± 10	92 ± 6	93 ± 7
Tilt						
0	95 ± 10	94 ± 12	94 ± 5	96 ± 11	95 ± 8	96 ± 14
1	96 ± 12	95 ± 11	94 ± 6	96 ± 11	97 ± 8	97 ± 16
2-5	97 ± 10	97 ± 9	96 ± 5	96 ± 10	98 ± 9	100 ± 11
6-10	97 ± 11	97 ± 9	97 ± 5	97 ± 12	99 ± 10	99 ± 10
11-15	96 ± 13	96 ± 9	95 ± 6	97 ± 13	95 ± 11	99 ± 10
Recovery						
0	92 ± 11	94 ± 10	94 ± 9	96 ± 9	93 ± 9	96 ± 8
1	94 ± 11	97 ± 9	95 ± 7	96 ± 7	93 ± 8	95 ± 7
2-5	94 ± 11	96 ± 9	94 ± 7	95 ± 9	94 ± 8	97 ± 8
6-10	93 ± 11	96 ± 9	93 ± 6	94 ± 9	96 ± 8	97 ± 10
11-15	94 ± 12	96 ± 10	93 ± 6	93 ± 9	96 ± 8	97 ± 9
Total Peripheral Resistance (dyne sec•cm ⁻⁵)						
Rest	2616±583	2508± 594	2527±504	2252±609	2504± 603	2769±612
Tilt						
0	3436±759	3231± 902	3139±643	2963±813	2767± 360	2998±594
1	3128±668	3281± 782	3152±679	2918±771	2958± 682	2967±589
2-5	3454±649	3315± 721	3176±616	2990±722	2979± 668	3178±552
6-10	3323±686	3142± 831	3181±601	2885±569	2912± 583	3069±491
11-15	3161±598	3136± 703	3092±607	2683±434	2864± 724	2971±628
Recovery						
0	2424±492	2389± 890	2397±800	2146±459	2372± 778	2784±716
1	2579±541	2628± 867	2584±572	2150±389	2276± 645	2690±375
2-5	2762±538	2733± 914	2626±400	2384±483	2736± 819	3044±453
6-10	2954±715	2715±1051	2710±486	2444±560	2758± 798	3282±812
11-15	3034±817	2909±1047	2762±583	2418±606	2978±1111	3029±724

Values are mean ± S.D.

Table 4-11. Effect of Training on Supine Resting Heart Rate, Stroke Volume, Cardiac Output, Blood Pressure, and Total Peripheral Resistance Measurements for Control, Treadmill, and Treadmill/Resistance Groups Before (T1) and After (T3) 6 months of Exercise Training.

Test	HR (b•min ⁻¹)	SV (ml)	\dot{Q} (L•min ⁻¹)	SBP (mmHg)	DBP (mmHg)	MAP (mmHg)	TPR *
CONT (<u>n</u> = 9)							
T1	61.6± 6.0	50.1±10.4	3.05±0.57	124± 9	77±8	92± 8	2561±583
T3	61.0± 5.2	51.3±12.2	3.09±0.65	122±11	78±7	92± 8	2508±594
TREAD (<u>n</u> = 14)							
T1	68.5±10.0	45.7± 7.3	3.13±0.69	127±12	79±4	95± 6	2528±504
T3	64.8± 9.5	55.1±10.5†	3.55±0.88†	135±20	75±7	95±10	2252±609†
TREAD/RESIST (<u>n</u> = 10)							
T1	61.7±10.7	50.9±13.0	3.08±0.69	122± 9	77±6	92± 6	2504±603
T3	60.4±10.6	47.3±10.3	2.80±0.53†	126±17	77±4	93± 7	2769±612†

*dyne sec•cm⁻⁵; † $p \leq 0.05$, change from respective T1 value
Values are mean ± S.D.

HR = Heart rate; SV = Stroke volume; \dot{Q} = Cardiac output; SBP = Systolic blood pressure; DBP = Diastolic blood pressure; MAP = Mean arterial pressure; TPR = Total peripheral resistance
CONT = Control; TREAD = Treadmill; TREAD/RESIST = Treadmill/Resistance.

The effect of training on resting SV and \dot{Q} was also investigated using 2 X 3 (test X group) ANOVA. The probability of a *type I* error in detecting a *test X group* interaction for resting SV was very low ($p < 0.01$), indicating that group assignment affected resting SV. Further analysis using a one-way ANOVA for each group showed that TREAD increased resting SV by 9.4 ml (20.6%) as a result of training ($p < 0.01$) (Table 4-11). The *type I* error rate for detecting a change in SV from T1 to T3 in TREAD/RESIST was 9.4%. In absolute terms, resting SV of TREAD/RESIST decreased by 3.6 ml (7.1%). The

differences between T1 and T3 resting SV values for CONT were due to random variation ($p = 0.73$).

Analysis of resting \dot{Q} data from T1 and T3 showed that there was a *test X group* interaction ($p < 0.01$). Further analysis using a one-way repeated measures ANOVA for each group indicated that TREAD increased resting \dot{Q} by $0.42 \text{ L} \cdot \text{min}^{-1}$ (13.4%) after 6 months of training ($p = 0.01$) while TREAD/RESIST showed a decline of $0.28 \text{ L} \cdot \text{min}^{-1}$ (9.1%; $p = 0.03$) (Table 4-11). Any differences between the T1 and T3 resting \dot{Q} values for CONT were due to random variation ($p = 0.81$). The greater \dot{Q} for TREAD was due to the increase in SV since resting HR was decreased by $3.7 \text{ b} \cdot \text{min}^{-1}$. On the other hand, the decline in resting \dot{Q} in TREAD/RESIST was due to a 7.1% decrease in SV as well as a 2.2% decrease in HR.

The probability of a *type I* error in detecting a *test X group* interaction in TPR was 0.02. Further analysis indicated that TREAD decreased resting TPR by 10.9% ($276 \text{ dyne sec} \cdot \text{cm}^{-5}$; $p = 0.05$) while TREAD/RESIST increased resting TPR by 10.6% ($265 \text{ dyne sec} \cdot \text{cm}^{-5}$, $p = 0.04$) (Table 4-11). Any differences between the T1 and T3 resting TPR values for CONT were due to random variation ($p = 0.96$). The decrease in resting TPR for TREAD was associated with a greater resting \dot{Q} , while the increase in resting TPR for TREAD/RESIST was associated with a decline in resting \dot{Q} . The repeated measures analyses for the resting BP variables indicated that training did not affect these measurements. *Type I* error rates in detecting *test X group* interactions were $p = 0.37$, 0.14 , and 0.89 for resting SBP, DBP, and MAP, respectively.

Effect of Training on the Cardiovascular Responses to Tilt

Using the averaged resting, tilt and recovery values, a 2 X 3 X 11 (test X group X time) repeated measures ANOVA was used to compare the rest, TILT and REC HR, SV, \dot{Q} , SBP, DBP, MAP, and TPR values. The overall Wilks' Lambda *type I* error rate generated for each effect and interaction is listed in Table 4-12. The *p*-value for a *test* effect for HR (*p* = 0.03) suggested that there was a systematic difference between T1 and T3 in this variable; further analysis showed that the mean HR at T1 was $68.0 \pm 11.0 \text{ b} \cdot \text{min}^{-1}$ while it decreased 2.9% ($2.0 \text{ b} \cdot \text{min}^{-1}$) to $66.0 \pm 9.7 \text{ b} \cdot \text{min}^{-1}$ at T3. This is similar in magnitude to the change seen in resting HR.

Table 4-12. Wilks' Lambda Values for 2 X 3 X 11 (Test X Group X Time) Repeated Measures Analysis for Heart Rate, Stroke Volume, Cardiac Output, Blood Pressure, and Peripheral Resistance Responses to 70° Head-up Tilt.

Effect†	HR	SV	\dot{Q}	SBP	DBP	MAP	TPR
Tst	0.03	0.13	0.53	0.08	0.30	0.49	0.81
Tst X G	0.29	0.02	0.02	0.76	0.66	0.96	0.01
Tm	<0.01	<0.01	<0.01	0.02	0.06	0.12	<0.01
Tm X G	0.75	0.87	0.89	0.08	0.15	0.25	0.81
Tst X Tm	0.56	0.39	0.33	0.94	0.38	0.86	0.75
Tst X Tm X G	0.48	0.16	0.26	0.38	0.56	0.99	0.42

† Tst = Test; Tm = Time; G = Group

HR = Heart rate; SV = Stroke volume, \dot{Q} = Cardiac output, SBP = Systolic blood pressure; DBP = Diastolic blood pressure; MAP = Mean arterial pressure; TPR = Total peripheral resistance.

The *p*-values for *test X group* interactions for SV and \dot{Q} (*p* < 0.01 and *p* < 0.01, respectively) suggest an effect of training on these variables. Further

analysis using a one-way repeated measures ANOVA for each group showed that TREAD increased average test SV 5.9 ml (15.0%) from 39.3 ± 5.1 ml at T1 to 45.2 ± 9.0 ml at T3 ($p = 0.01$). The 3.1 ml (6.7%) decrease in the average SV measurement of TREAD/RESIST was due to random variation ($p = 0.15$): the T1 and T3 values were 46.2 ± 12.1 ml and 43.1 ± 9.3 ml, respectively. Changes in the average SV of CONT were also due to random variation ($p = 0.47$): the T1 and T3 values were 42.6 ± 7.4 ml at T1 and 44.4 ± 8.5 ml, respectively (Figure 4-1).

The post hoc analysis of the \dot{Q} data (one-way ANOVA by group) showed that TREAD increased average test \dot{Q} after 6 months of training: the T1 mean test value was 2.80 ± 0.52 L•min⁻¹ while the mean T3 value increased to 3.06 ± 0.63 L•min⁻¹ ($\Delta = 0.26$ L•min⁻¹, +9.3%; $p = 0.04$). Average test \dot{Q} decreased in TREAD/RESIST from 2.95 ± 0.54 L•min⁻¹ at T1 to 2.66 ± 0.32 L•min⁻¹ at T3 ($\Delta = 0.29$ L•min⁻¹, -9.8%, $p = 0.05$). The changes from T1 to T3 in average \dot{Q} for CONT were due to random variation. The control group had a T1 value of 2.67 ± 0.34 L•min⁻¹, while the T3 value was 2.78 ± 0.39 L•min⁻¹ ($p = 0.48$) (Figure 4-1). The percent changes in average test SV and \dot{Q} are illustrated in Figure 4-2.

A further analysis of the change in SV and \dot{Q} from rest to tilt was done in a 2 X 3 (test X group) repeated measures ANOVA using both the absolute and relative differences between the mean resting value and the mean tilt value. Results of these analyses are listed in Table 4-13. The decline in SV from rest to tilt in TREAD increased from 12.0 ± 7.6 ml at T1 to 17.7 ± 6.6 ml at T3; the relative decline was also increased from $25.0 \pm 14.3\%$ at T1 to $31.5 \pm 7.6\%$ at T3. Any changes for CONT and TREAD/RESIST in the relative ($p = 0.79$ and 0.37 , respectively) or absolute ($p = 0.73$ and 0.25 , respectively) declines in SV could be accounted for by random variation.

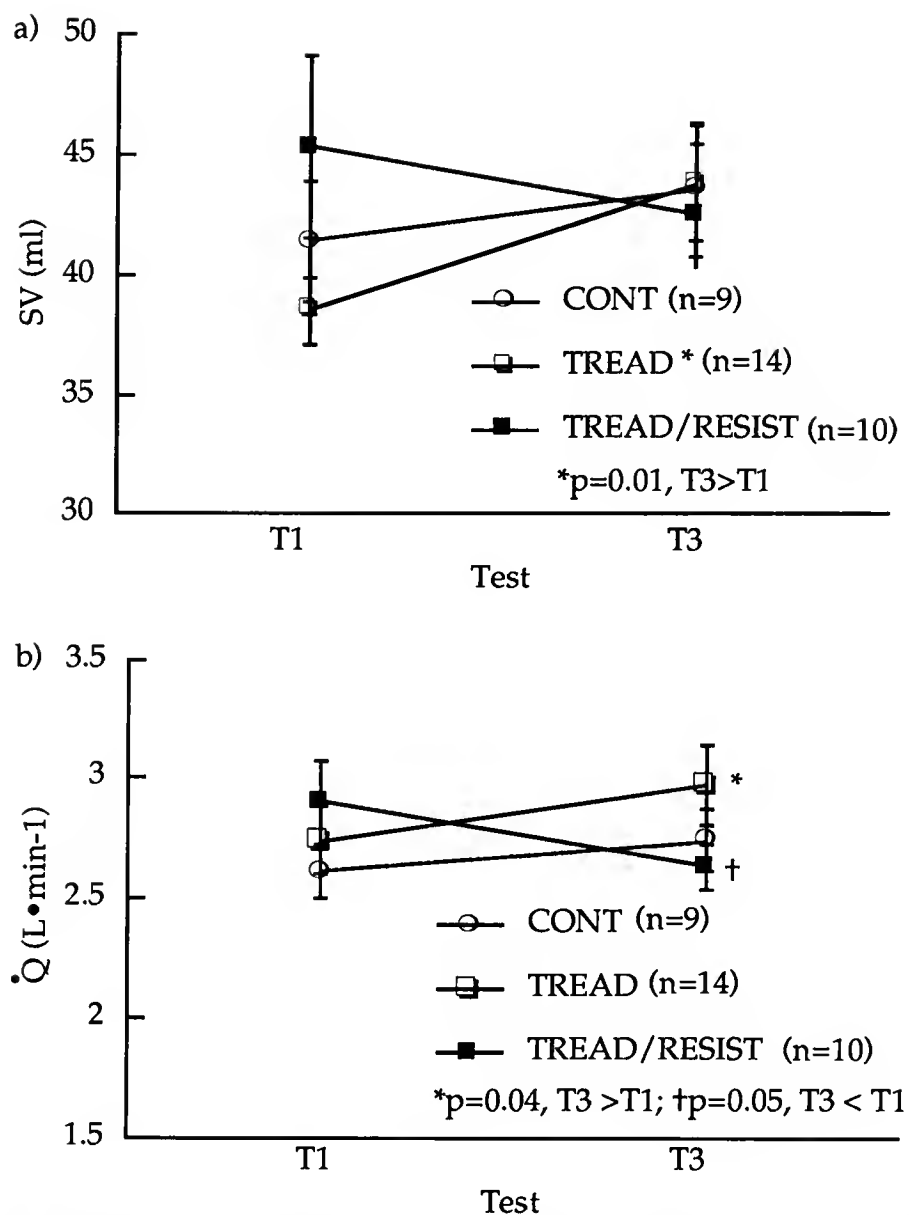


Figure 4-1. Mean test responses of control (CONT), treadmill (TREAD), and treadmill/resistance (TREAD/RESIST) groups to 70° head-up tilt before (T1) and after (T3) 6 months of exercise training: a) stroke volume (SV); b) cardiac output (\dot{Q}).

A similar change took place for the absolute decline in \dot{Q} . The decline in \dot{Q} at T1 for TREAD was $0.59 \pm 0.52 \text{ L} \cdot \text{min}^{-1}$; this increased to $0.86 \pm 0.51 \text{ L} \cdot \text{min}^{-1}$ at T3. The *type I* error rate for detecting a *time X group* interaction in the relative change in \dot{Q} was 0.11. The relative changes in \dot{Q} shown by

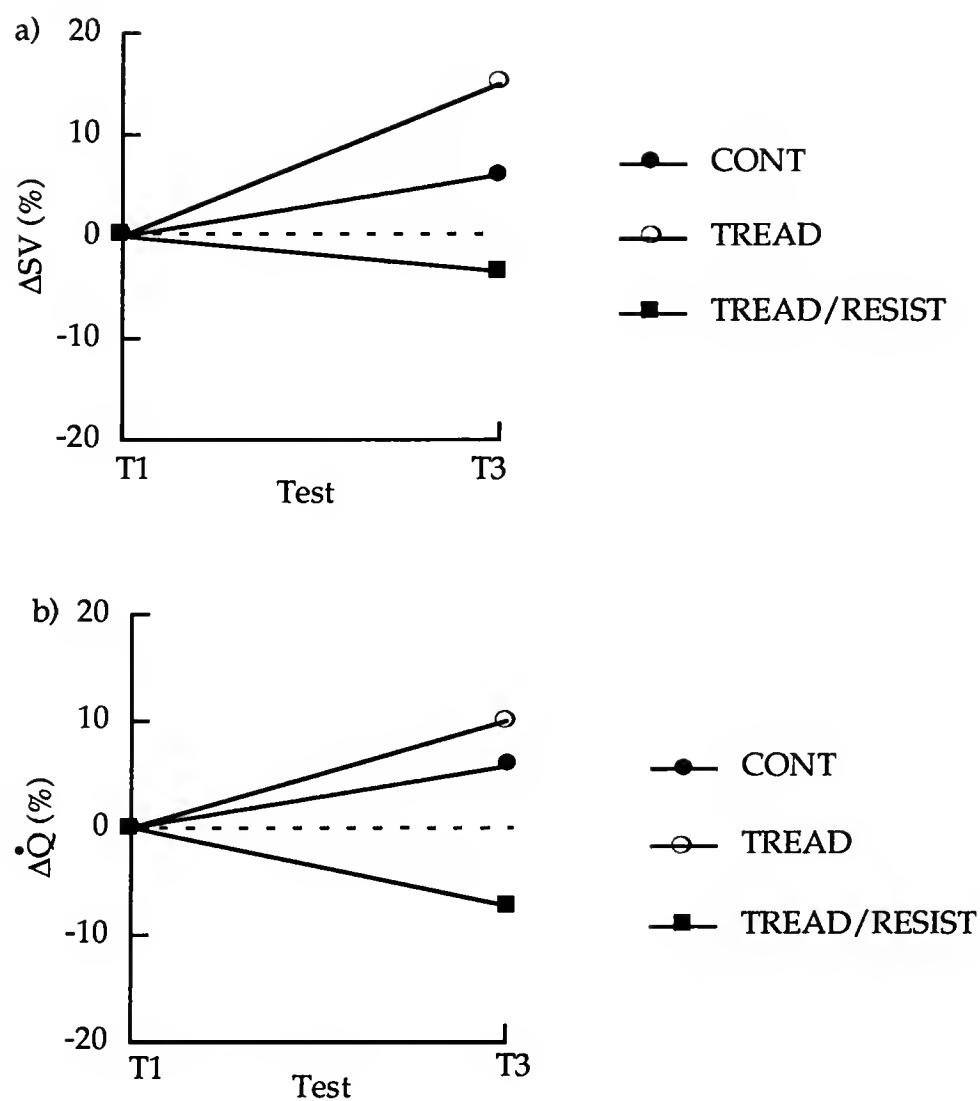


Figure 4-2. Percent change (Δ) in mean test response from prior to exercise training (T1) to after (T3) 6 months of exercise training in control (CONT), treadmill (TREAD), and treadmill/resistance (TREAD/RESIST) exercise groups: a) mean test stroke volume (SV) and b) mean test cardiac output (\dot{Q}).

TREAD at T1 and T3 were $17.3 \pm 15.1\%$ and $23.1 \pm 9.6\%$, respectively ($p = 0.08$). Any changes for CONT and TREAD/RESIST in the relative ($p = 0.70$ and 0.24 , respectively) or absolute ($p = 0.90$ and 0.21 , respectively) declines in \dot{Q} could be accounted for by random variation.

Table 4-13. Analysis of the Effect of 6 Months of Exercise Training on the Relative and Absolute Change in Stroke Volume and Cardiac Output from Rest to 70° Head-up Tilt for Control, Treadmill, and Treadmill/Resistance Groups.

Variable	Test X Group*	CONT† (<u>n</u> = 9)	TREAD† (<u>n</u> = 14)	TREAD/RESIST† (<u>n</u> = 10)
ΔSV_{\S}	0.01	0.73	<0.01	0.25
$\% \Delta SV^a$	0.07	0.79	0.03	0.37
$\Delta \dot{Q}_{\S}$	0.05	0.90	0.04	0.21
$\% \Delta \dot{Q}^a$	0.11	0.70	0.08	0.24

CONT = Control; TREAD = Treadmill; TREAD/RESIST = Treadmill/Resistance.

* Wilks' Lambda

† Single-degree-of-freedom contrast, analysis of mean difference (T1-T3)

§ Δ values calculated as (mean resting value - mean tilt value)

^a $\% \Delta$ values calculated as (Δ value/mean resting value)

The p-value for *test X group* interaction for TPR ($p = 0.01$; Table 4-12) suggested an effect of training on this variable. However, further analysis using a one-way repeated measures ANOVA for each group resulted in a high probability of a *type I* error in detecting a *test* effect for all groups ($p = 0.83, 0.20$, and 0.25 for CONT, TREAD, and TREAD/RESIST, respectively). The raw data show that TREAD decreased average test TPR by 199 dyne $\text{sec} \cdot \text{cm}^{-5}$ (7.0%) from 2843 ± 466 dyne $\text{sec} \cdot \text{cm}^{-5}$ at T1 to 2644 ± 637 dyne $\text{sec} \cdot \text{cm}^{-5}$ at T3. Average test TPR increased in TREAD/RESIST by 240 dyne $\text{sec} \cdot \text{cm}^{-5}$ (8.7%): the T1 and T3 values were 2749 ± 645 dyne $\text{sec} \cdot \text{cm}^{-5}$ and 2989 ± 446 dyne $\text{sec} \cdot \text{cm}^{-5}$, respectively. The change in average TPR of CONT was from 2973 ± 448 dyne $\text{sec} \cdot \text{cm}^{-5}$ at T1 to 2926 ± 617 dyne $\text{sec} \cdot \text{cm}^{-5}$ at T3 (47 dyne $\text{sec} \cdot \text{cm}^{-5}$, 1.6%).

To test the probability that changes during TILT and REC (*time* effect) in HR, SV, and \dot{Q} could be attributed to random experimental variation, a

repeated measures analysis comparing all levels of time to rest was performed for each variable. At each time point, values were averaged over tests and groups. The results of these analyses are shown in Table 4-14. For the HR analysis, there was a very low *type I* error rate for all time points during TILT; it was concluded that TILT caused an increase in HR. Heart rate initially accelerated $5.3 \text{ b} \cdot \text{min}^{-1}$ (8.3%), from a resting value of $63.5 \pm 9.3 \text{ b} \cdot \text{min}^{-1}$ to a value at TILT₀ of $68.8 \pm 12.7 \text{ b} \cdot \text{min}^{-1}$. There were further increases during TILT; the final HR value (TILT₁₁₋₁₅) was elevated $9.7 \text{ b} \cdot \text{min}^{-1}$ (15.2%) above the resting value. A further analysis of the trend during TILT showed that the HR increase, while slight, was progressive. A comparison of each level of time to the mean of subsequent levels yielded the following *type I* error rates: rest, $p < 0.01$; T₀, $p < 0.01$, T₁, $p = 0.06$, T₂₋₅, $p < 0.01$, and T₆₋₁₀, $p < 0.01$. The HR at REC₀ was elevated 6.5% ($4.1 \text{ b} \cdot \text{min}^{-1}$) above the resting value, but the large *type I* error rate at REC₁ indicated that the difference from rest at this time point could be accounted for by random variation. The HR fell below resting ($1.2\text{-}1.6 \text{ b} \cdot \text{min}^{-1}$; 1.9-2.5%) during the remainder of REC.

The analysis comparing all time levels of SV to rest showed that there was a very low *type I* error rate for all time points during TILT (Table 4-14); it was concluded that TILT caused an decrease in SV. Decreases in SV during TILT ranged from 11.9 ml (23.8%) to 13.6 ml (27.1%). The large *type I* error rate at REC₀ and REC₁ indicate that the differences from rest at these points could be due to random variation. However, the small *type I* error rates during the remainder of the time points during REC indicate that further supine rest (up to 15 minutes) caused a decrease in SV. Stroke volume declined 1.7 to 3.2 ml (3.3 to 6.4%) between minutes 2 and 15 of REC.

The low *type I* error rate during TILT for the \dot{Q} analysis comparing all time points to rest suggest that upright tilt caused a decrease in \dot{Q} ; decreases

Table 4-14. Post Hoc Analysis for *Time* Effect to Detect Changes in Heart Rate, Stroke Volume, and Cardiac Output as a Result of 70° Head-up Tilt (Means Averaged Over Tests and Groups).

Time	Heart Rate			p*	Stroke Volume			p*	Cardiac Output			p*
	Mean±SD (b•min ⁻¹)	Δ [†]	%Δ§		Mean±SD (ml)	Δ [†]	%Δ§		Mean±SD (L•min ⁻¹)	Δ [†]	%Δ§	
Rest	63.5 ± 9.3	--	--	--	50.1 ± 10.6	--	--	--	3.15 ± 0.71	--	--	--
Tilt												
0	68.8 ± 12.7	+5.3	+8.3	<0.01	38.2 ± 8.8	-11.9	-23.8	<0.01	2.56 ± 0.52	-0.59	-18.7	<0.01
1	70.7 ± 11.0	+7.2	+11.3	<0.01	36.9 ± 7.7	-13.2	-26.3	<0.01	2.60 ± 0.51	-0.55	-17.5	<0.01
2-5	70.4 ± 10.3	+6.9	+10.9	<0.01	36.5 ± 7.4	-13.6	-27.1	<0.01	2.54 ± 0.47	-0.61	-19.4	<0.01
6-10	71.4 ± 11.1	+7.9	+12.4	<0.01	36.8 ± 8.0	-13.3	-26.5	<0.01	2.59 ± 0.46	-0.56	-17.8	<0.01
11-15	73.2 ± 12.0	+9.7	+15.2	<0.01	37.1 ± 8.9	-13.0	-25.9	<0.01	2.64 ± 0.45	-0.51	-16.2	<0.01
Recovery												
0	67.6 ± 11.9	+4.1	+6.5	<0.01	49.6 ± 11.8	-0.5	-1.0	0.55	3.29 ± 0.77	+0.14	+4.4	0.03
1	64.2 ± 10.9	+0.7	+1.1	0.27	51.0 ± 11.9	+0.9	+1.8	0.25	3.22 ± 0.70	+0.12	+3.8	0.18
2-5	62.3 ± 10.2	-1.2	-1.9	0.04	48.4 ± 11.5	-1.7	-3.3	0.02	2.95 ± 0.61	-0.20	-6.3	<0.01
6-10	61.9 ± 9.7	-1.6	-2.5	0.01	47.0 ± 11.5	-3.1	-6.2	<0.01	2.85 ± 0.64	-0.30	-9.5	<0.01
11-15	62.3 ± 9.1	-1.2	-1.9	0.03	46.9 ± 12.0	-3.2	-6.4	<0.01	2.86 ± 0.67	-0.29	-9.2	<0.01

* Comparison to resting value

† Δ = Change from rest

§ %Δ = Percent change from rest

during TILT ranged from 0.51 to 0.61 L•min⁻¹ (16.2 to 19.4%). At REC₀, \dot{Q} was elevated by 0.14 L•min⁻¹ (4.4%), but the large *type I* error rate at REC₁ ($p = 0.18$) indicated that the difference from rest at this time point could be due to random variation. Decline in \dot{Q} during the remainder of REC ranged from 0.20 to 0.30 L•min⁻¹ (6.3% to 9.5%) (Table 4-14).

The overall multivariate analysis for both SBP and DBP showed a small probability of a *type I* error in detecting a *time* effect ($p = 0.02$, and 0.06 , respectively) (Table 4-15). In the post-hoc analyses comparing all time points to rest, the small p -value for SBP at TILT₀ indicated that initiation of tilt caused a reduction in SBP. However, the reduction was small (3 mmHg, 2.3%) (Table 4-15). The large *type I* error rates generated for the other time points during TILT indicate that any differences from rest in SBP was due to random variation. It can be concluded that SBP is well maintained during TILT in healthy older persons. The small *type I* error rates generated for SBP at REC₀, REC₁, and REC₂₋₅ indicated that SBP was slightly (1-2 mmHg, 1- 2%) elevated for up to 5 minutes after upright tilt. However, it should be noted that the mean values at these time points were similar to the value at TILT₁₀, for which a large probability of a *type I* error rate was obtained.

The post hoc *time* analysis for DBP showed a small probability for a *type I* error at all time points during TILT (Table 4-15). It can be concluded, therefore, that upright tilt caused an increase in DBP. Increases during tilt averaged 4-5 mmHg (5-7%). The large p -values generated for DBP during REC suggest that any differences from rest were due to random variation. Therefore, after upright tilt, DBP rapidly recovers to near resting values.

The overall multivariate test for MAP indicated an 11.9% probability of a *type I* error in detecting a *time* effect (Table 4-12). Therefore, further analyses were not done. Inspection of the raw data (Table 4-15) show that upright tilt

Table 4-15. Post Hoc Analysis for *Time* Effect to Detect Changes in Systolic, Diastolic, and Mean Arterial Pressure as a Result of 70° Head-up Tilt (Means Averaged Over Tests and Groups).

Time	Systolic Blood Pressure			Diastolic Blood Pressure			Mean Arterial Pressure		
	Mean±SD (mmHg)	Δ† %	Δ§ p*	Mean±SD (mmHg)	Δ† %	Δ§ p*	Mean±SD (mmHg)	Δ† %	Δ§ p*
Rest	127 ± 14	--	--	77 ± 6	--	--	93 ± 8	--	--
Tilt									
0	124 ± 16	-3	-2.4	81 ± 9	+4	+5.2	95 ± 10	+2	+2.2
1	125 ± 17	-2	-1.6	81 ± 9	+4	+5.2	96 ± 10	+3	+3.2
2-5	128 ± 15	+1	+0.8	82 ± 8	+5	+6.5	97 ± 9	+4	+4.3
10	129 ± 17	+2	+1.6	82 ± 8	+5	+6.5	98 ± 9	+5	+5.4
15	126 ± 17	-1	-0.8	81 ± 8	+4	+5.2	96 ± 10	+3	+3.2
Recovery									
0	128 ± 16	+1	+0.8	78 ± 7	+1	+1.3	94 ± 9	+1	+1.1
1	129 ± 14	+2	+1.6	78 ± 7	+1	+1.3	95 ± 8	+2	+2.2
2-5	129 ± 14	+2	+1.6	79 ± 7	+2	+2.6	95 ± 8	+2	+2.2
10	128 ± 16	+1	+0.8	78 ± 7	+1	+1.3	95 ± 8	+2	+2.2
15	127 ± 15	+0	+0.0	79 ± 7	+2	+2.6	95 ± 9	+2	+2.2

†Value - rest

§(Value - rest)/rest

*Comparison to resting

NC = Not calculated (see text)

caused a slight increase in MAP which was 2 mmHg (2.2%) initially, with further small increases to 5 mmHg (5.4%) during the remainder of TILT. The decreases in SBP at TILT₀ and TILT₁ are responsible for the slightly attenuated initial response of MAP. Differences from rest during REC were less than 2.2% (1-2 mmHg).

Table 4-16. Post Hoc Analysis for *Time* Effect to Detect Changes in Total Peripheral Resistance as a Result of 70° Head-up Tilt (Means Averaged Over Tests and Groups).

Time	Mean ± S.D. (dyne sec•cm ⁻⁵)	Δ *	%Δ†	p**
Rest	2478 ± 627	---	---	---
TILT 0	3052 ± 761	+574	+23.2	<0.01
TILT 1	3041 ± 718	+563	+22.7	<0.01
TILT 2-5	3140 ± 665	+662	+26.7	<0.01
TILT 10	3015 ± 622	+537	+21.7	<0.01
TILT 15	2913 ± 599	+435	+17.6	<0.01
REC 0	2413 ± 689	-65	-2.6	0.07
REC 1	2445 ± 603	-33	-1.3	0.44
REC 2-5	2688 ± 667	+210	+8.5	<0.01
REC 10	2851 ± 858	+373	+15.1	<0.01
REC 15	2757 ± 816	+279	+11.3	<0.01

* Value - rest

† (Value - rest)/rest

** Comparison to rest

The analysis comparing all time levels of TPR to rest showed that there was a very low *type I* error rate for all time points during TILT (Table 4-16); it was concluded that TILT caused an increase in TPR. Increases in TPR during TILT ranged from 435 dyne sec•cm⁻⁵ (17.6%) to 662 dyne sec•cm⁻⁵ (26.7%). The *type I* error rate at REC₀ was 0.07; however, the difference from rest was small at this point (65 dyne sec•cm⁻⁵, 2.6%). The large *type I* error rate at REC₁

indicates that the difference from rest at this point was due to random variation. The small *type I* error rates generated for remainder of the time points during REC indicate that further supine rest (up to 15 minutes) caused an increase in TPR. Resistance was elevated between 212 and 373 dyne $\text{sec} \cdot \text{cm}^{-5}$ (8.5 to 15.1%) between minutes 2 and 15 of REC. The elevation in TPR was associated with a decline in \dot{Q} during this period.

Hormonal and Plasma Volume Response to Training and Tilt

Plasma volume measurements were obtained in 18 subjects (CONT $n = 7$; TREAD $n = 4$; TREAD/RESIST $n = 7$) from the main sample of 33. A repeated measures analysis with four levels of time (pre-tilt and tilt at both T1 and T3) showed no *time X group* interaction for either PV ($p = 0.72$) or BV (0.84). Therefore, data from TREAD and TREAD/RESIST were combined into a single group (TRAIN).

An initial analysis of resting PV and BV was done in a 2 X 2 (group X time) repeated measures ANOVA. The time measurements represented only the pre-tilt measurements at T1 and T3. Therefore, subjects who were eliminated from the main sample of 33 because they fainted during the T1 tilt test or because of medical conditions which may have affected their cardiovascular responses to tilt were included in this analysis of resting PV and BV responses. The results indicated that TRAIN ($n = 15$) increased PV by 300 ml (11.0%) from 2731 ± 674 ml at T1 to 3031 ± 939 ml at T3 ($p = 0.04$), while BV increased 501 ml (12.2%) from 4114 ± 1050 ml at T1 to 4616 ± 1499 ml at T3 ($p = 0.07$). The T1 and T3 measurements of PV for CONT ($n = 9$) were 2734 ± 510 ml and 2723 ± 652 ml, respectively, while the respective BV measurements were 4164 ± 900 ml and 4248 ± 1149 ml.

For the remainder of the analyses, the sample of 18 was used. The responses of plasma volume and related variables to training and tilt for this sample are shown in Table 4-17. The *type I* error rate generated by a one-way ANOVA indicated that group differences in T1 pre-tilt values for PV ($p = 0.86$), BV (0.91), and RCV (0.99) were due to random variation.

Table 4-17. Responses of Plasma Volume, Blood Volume, and Red Cell Volume to 70° Head-up Tilt Before (T1) and After (T3) 6 Months of Exercise Training in the Control and Exercise Training Groups ($n = 18$).

	T1		T3	
	Pre-tilt	Tilt	Pre-tilt	Tilt
CONT ($n = 7$)				
PV (ml)	2752 ± 586	2128 ± 403	2704 ± 750	2162 ± 532
BV (ml)	4166 ± 1039	3643 ± 805	4229 ± 1323	3791 ± 1108
RCV (ml)	1415 ± 474	1514 ± 413	1524 ± 591	1630 ± 613
TRAIN ($n = 11$)				
PV (ml)	2691 ± 742	2165 ± 558	2947 ± 957	2434 ± 972
BV (ml)	4107 ± 1149	3649 ± 960	4499 ± 1498	4177 ± 1625
RCV (ml)	1415 ± 421	1484 ± 436	1552 ± 552	1743 ± 673
Overall ($n = 18$)				
PV (ml)	2715 ± 668	2151 ± 491	2853 ± 867	2328 ± 821
BV (ml)	4130 ± 1077	3647 ± 878	4394 ± 1399	4027 ± 1423
RCV (ml)	1415 ± 429	1496 ± 415	1541 ± 550	1699 ± 634

Values are mean ± S.D.

CONT = Control; TRAIN = Exercise-training (Treadmill + Treadmill/Resistance Groups); PV = Plasma volume; BV = Blood volume; RCV = Red cell volume.

Analyses of changes in PV, BV, and RCV were done in a 4 X 2 (time X group) repeated measures ANOVA where the four time points used were pre-tilt and tilt at both T1 and T3. The results of these analyses are shown in Table 4-18. The analysis for PV indicated that there was a decrease in PV

during tilt at both T1 and T3 ($p < 0.01$) that was not affected by group assignment ($p = 0.41$ for *time X group* interaction). Decreases averaged 20.8% and 18.4% for T1 and T3, respectively.

Table 4-18. Probabilities for *Type I* Error in Detecting a Change in Plasma Volume, Blood Volume and Red Cell Volume as a Result of 70° Head-up Tilt or Exercise Training.

	Group by Time*	Time*	Pre-tilt T1 to Pre-tilt T3†	Tilt T1 to Tilt T3†	Pre-tilt T1 to Tilt T1†	Pre-tilt T3 to Tilt T3†
PV	0.41	<0.01	0.31	0.21	<0.01	<0.01
BV	0.58	<0.01	0.15	0.09	<0.01	<0.01
RCV	0.58	<0.01	0.05	0.03	<0.01	<0.01

* Wilks' Lambda

† Single-degree-of-freedom contrast, analysis of mean difference

PV = Plasma volume; BV = Blood volume; RCV = Red cell volume.

Differences between the T1 and T3 pre-tilt ($p = 0.31$) or tilt ($p = 0.21$) PV values were due to random variation. Although TRAIN increased resting PV by 9.5% (256 ml), the *type I* error rate for the *time X group* interaction indicated this change was not different from the 1.7% (48 ml) decrease seen in CONT. Despite the increase by TRAIN, the decreases in PV during tilt for TRAIN were nearly identical on an absolute basis (526 and 513 ml for T1 and T3, respectively). The absolute PV during tilt at T3 was 269 ml (12.4%) greater than the T1 tilt measurement and only 9.6% lower than the resting T1 value.

The analysis of BV showed similar results (Table 4-18). There were decreases in BV during tilt at both T1 (483 ml, 11.7%) and T3 (367 ml, 8.3%) ($p < 0.01$), while differences between the two pre-tilt BV values were due to

random variation ($p = 0.15$). The *type I* error rate of 0.09 for the relationship between the T1 and T3 tilt values indicates that there may have been a systematic increase in the BV measurements during tilt. The average T1 tilt measurement was 3647 ± 878 ml while the T3 measurement was increased 10.4% to 4027 ± 1423 ml. Group assignment did not appear to affect BV changes, as evidenced by the large *type I* error rate generated for the *group X time* interaction ($p = 0.58$).

Although TRAIN increased resting BV by 9.5% (392 ml), the *type I* error rate for the *time X group* interaction indicated this change was not different from the 1.5% (63 ml) increase seen in CONT. The absolute BV during tilt for TRAIN at T3 was 528 ml (14.5%) greater than the T1 tilt BV and 70 ml greater than the resting T1 BV. Red cell volume increased during tilt at both T1 ($p < 0.01$) and T3 ($p < 0.01$) (Table 4-18). There were increases in both resting ($p = 0.05$) and tilt ($p = 0.03$) RCV from T1 to T3; however, these were not related to group assignment ($p = 0.58$ for overall *time X group* interaction).

The responses of Hb and Hct to training and tilt are shown in Table 4-19. A one-way ANOVA on the T1 pre-tilt values indicate that any initial group differences were due to random variation ($p = 0.72$ and 0.50 for Hb and Hct, respectively). Analyses of the Hb and Hct responses to tilt and training were done in a 4×2 (*time X group*) repeated measures ANOVA where the measures of time were pre-tilt and tilt at both T1 and T3. The results of these analyses are shown in Table 4-20. Both Hb and Hct increased during tilt at T1 and T3 ($p < 0.01$); the changes were not group related ($p = 0.24$ and $p = 0.39$ for Hb and Hct, respectively, for overall *time X group* interaction). Differences between the T1 and T3 resting Hct values were due to random variation ($p = 0.12$). However, the *type I* error rate for the differences between the T1 and T3

tilt Hct values ($p = 0.07$) indicated a systematic change in the tilt Hct values; the average tilt value at T1 was $40.2 \pm 3.8\%$ while the average T3 tilt value was $41.5 \pm 3.2\%$.

Table 4-19. Hemoglobin and Hematocrit Measurements at Rest and During 70° Head-up Tilt Before (T1) and After (T3) 6 Months of Exercise Training in Control and Exercise Training Groups ($n = 18$).

Group		Hematocrit		Hemoglobin	
		Pre-tilt	Tilt	Pre-tilt	Tilt
CONT ($n = 7$)	T1	36.8±4.3	41.1±2.7	13.2±1.7	15.0±2.3
	T3	38.6±4.2	42.1±4.7	13.4±1.6	14.9±1.8
TRAIN ($n = 11$)	T1	37.7±2.4	40.4±3.5	13.0±0.8	14.6±1.3
	T3	37.8±2.4	41.7±2.4	14.2±0.8	15.5±0.9

Values are mean \pm S.D.

CONT = Control; TRAIN = Combined (Treadmill + Treadmill/Resistance) training group

The low *type I* error rate associated with the change in resting Hb from T1 to T3 ($p < 0.01$) indicated a systematic change between these two time points. Mean resting values of Hb increased from T1 (12.9 ± 1.4 mg/dl) to T3 (13.9 ± 1.1 mg/dl); this change was not group related ($p = 0.24$ for overall *time X group* interaction). However, changes in Hb during tilt from T1 to T3 were due to random variation ($p = 0.21$).

The percent change in PV, BV, and RCV during tilt at T1 and T3 was calculated and is shown for each group in Table 4-21. The large *type I* error rate for a *test X group* interaction generated by the 2 X 2 (test X group) ANOVA indicated that any group differences in the percent change in PV between T1 and T3 were due to random variation ($p = 0.53$). Similarly, *p*-values for *test X group* interactions in the percent change in BV ($p = 0.99$) and

RCV ($p = 0.10$) during tilt at T1 and T3 indicated random variation could account for group differences.

Table 4-20. Probabilities for *Type I* Error in Detecting a Change in Hemoglobin and Hematocrit as a Result of 70° Head-up Tilt Before (T1) or After (T3) 6 Months of Exercise Training.

	Group by Time*	Time*	Pre-tilt T1 to Pre-tilt T3†	Tilt T1 to Tilt T3†	Pre-tilt T1 to Tilt T1†	Pre-tilt T3 to Tilt T3†
Hb	0.24	<0.01	<0.01	0.21	<0.01	<0.01
Hct	0.39	<0.01	0.12	0.07	<0.01	<0.01

* Wilks' Lambda

† Single-degree-of-freedom contrast, analysis of mean difference

Hb = Hemoglobin; Hct = Hematocrit.

Table 4-21. Percent Change in Plasma Volume, Blood Volume, and Red Cell Volume During 70° Head-up Tilt Before (T1) and After (T3) 6 months of Exercise Training in the Control and Exercise Training Groups ($n = 18$).

Group		Δ PV (%)	Δ BV (%)	Δ RCV (%)
CONT ($n = 7$)	T1	-22.2 ± 4.2	-11.9 ± 4.4	9.8 ± 13.1
	T3	-19.4 ± 4.2	-9.7 ± 4.3	7.7 ± 7.1
TRAIN ($n = 11$)	T1	-18.9 ± 6.5	-10.6 ± 5.2	5.1 ± 6.1
	T3	-18.6 ± 7.3	-8.4 ± 5.6	11.4 ± 6.9

Values are mean \pm S.D.

CONT = Control; TRAIN = Combined training group (Treadmill + Treadmill/Resistance).

Δ PV = Change in plasma volume from supine rest to 70° head-up tilt.

Δ BV = Change in blood volume from supine rest to 70° head-up tilt.

Δ RCV = Change in red cell volume from supine rest to 70° head-up tilt.

Hormone/electrolyte analyses were done on a sample of 27. Analyses were initially performed using a 4 X 3 (time X group) repeated measures design in order to determine if group assignment affected the response to tilt or training. The four levels of time consisted of the measurements at pre-tilt and tilt at both T1 and T3. *Time X group* interactions for the various analyses were as follows: ALDO, $p = 0.53$; AVP, $p = 0.43$; K^+ , $p = 0.86$; Na^+ , $p = 0.30$; PRO, $p = 0.99$; NE, $p = 0.50$; and EPI, $p = 0.46$. It can be concluded that any differences among the groups across the four levels of time were due to random variation. Therefore, because of the necessity for combining the training groups for PV analyses and because of the relationship between hormones/electrolytes and fluid volume control, data for TREAD and TREAD/RESIST were combined into a single group (TRAIN) for these hormone/electrolyte analyses.

However, the *time X group* interaction for the ACTH analysis yielded a *type I* error rate of 0.03. Follow up analyses indicated that there were group differences in the response to tilt at T3: CONT had an increase in ACTH during tilt at T3 from a resting value of $57.5 \pm 47.5 \text{ pg} \cdot \text{ml}^{-1}$ to a tilt value of $84.5 \pm 52.8 \text{ pg} \cdot \text{ml}^{-1}$ ($p = 0.01$). The change in ACTH from rest to tilt at T3 for TREAD was from $69.6 \pm 36.2 \text{ pg} \cdot \text{ml}^{-1}$ to $49.3 \pm 31.2 \text{ pg} \cdot \text{ml}^{-1}$, respectively ($p = 0.07$) while the change from rest to tilt for TREAD/RESIST was from $44.1 \pm 24.8 \text{ pg} \cdot \text{ml}^{-1}$ to $58.7 \pm 32.6 \text{ pg} \cdot \text{ml}^{-1}$, respectively ($p = 0.20$). The *type I* error rate for detection of a change in ACTH as a result of tilt at T1 was 0.54, while comparisons of the T1 and T3 resting values, and of the T1 and T3 tilt values yielded a *type I* error rates of 0.28 and 0.17, respectively.

Table 4-22. Hormonal/Electrolyte Response to 70° Head-up Tilt Before and After 6 Months of Exercise Training in the Control and Exercise Training Groups (\underline{n} = 27).

	Pre-training		Post-training	
	Rest	Tilt	Rest	Tilt
ACTH (pg•ml ⁻¹)				
CONT (\underline{n} = 7)	35.1 ± 12.4	46.8 ± 26.5	57.5 ± 47.5	84.5 ± 52.8
TRAIN (\underline{n} = 20)	54.8 ± 32.4	54.6 ± 43.7	56.9 ± 32.9	53.9 ± 30.9
Overall (\underline{n} = 27)	50.2 ± 30.0	52.8 ± 40.0	57.1 ± 35.7	61.0 ± 38.2
ALDO (pg•ml ⁻¹)				
CONT (\underline{n} = 7)	57.4 ± 29.1	72.2 ± 28.6	61.5 ± 43.4	69.4 ± 58.3
TRAIN (\underline{n} = 20)	57.3 ± 31.3	67.9 ± 42.4	58.5 ± 36.4	70.8 ± 53.5
Overall (\underline{n} = 27)	57.3 ± 30.2	69.0 ± 38.8	59.3 ± 37.5	70.5 ± 53.6
AVP (pg•ml ⁻¹)				
CONT (\underline{n} = 7)	2.5 ± 3.0	2.5 ± 2.6	2.3 ± 1.9	3.1 ± 4.0
TRAIN (\underline{n} = 20)	2.5 ± 2.8	4.3 ± 2.5	1.6 ± 1.2	1.8 ± 2.0
Overall (\underline{n} = 27)	2.5 ± 2.8	3.9 ± 3.8	1.7 ± 1.4	2.2 ± 2.6
K ⁺ (mEq•L ⁻¹)				
CONT (\underline{n} = 4)	4.2 ± 0.2	4.4 ± 0.3	4.3 ± 0.3	4.4 ± 0.2
TRAIN (\underline{n} = 13)	4.1 ± 0.4	4.3 ± 0.3	4.3 ± 0.5	4.4 ± 0.4
Overall (\underline{n} = 17)	4.1 ± 0.3	4.3 ± 0.3	4.2 ± 0.4	4.4 ± 0.3
Na ⁺ (mEq•L ⁻¹)				
CONT (\underline{n} = 7)	141.5 ± 2.2	141.3 ± 2.9	141.7 ± 3.5	141.9 ± 2.6
TRAIN (\underline{n} = 20)	140.0 ± 1.8	140.5 ± 2.9	140.8 ± 3.2	141.4 ± 3.0
Overall (\underline{n} = 27)	140.4 ± 2.0	140.7 ± 2.9	141.1 ± 3.2	141.5 ± 2.8
PROT (mg•dl ⁻¹)				
CONT (\underline{n} = 7)	8.2 ± 0.7	9.0 ± 0.7	8.6 ± 0.4	9.5 ± 0.3
TRAIN (\underline{n} = 20)	8.2 ± 0.7	9.0 ± 0.7	8.6 ± 0.4	9.5 ± 0.5
Overall (\underline{n} = 27)	8.2 ± 0.7	9.0 ± 0.7	8.6 ± 0.4	9.5 ± 0.5
NE (pg•ml ⁻¹)				
CONT (\underline{n} = 6)	436 ± 140	636 ± 254	300 ± 112	585 ± 191
TRAIN (\underline{n} = 20)	517 ± 186	780 ± 306	389 ± 139	712 ± 213
Overall (\underline{n} = 26)	498 ± 178	747 ± 297	368 ± 136	683 ± 212
EPI (pg•ml ⁻¹)				
CONT (\underline{n} = 6)	6.3 ± 15.5	21.7 ± 36.3	0.0 ± 0.0	17.3 ± 26.9
TRAIN (\underline{n} = 20)	29.7 ± 56.4	11.9 ± 30.2	9.1 ± 19.6	22.4 ± 38.2
Overall (\underline{n} = 26)	24.3 ± 50.6	14.1 ± 31.2	7.0 ± 17.5	21.2 ± 35.5

Values are mean ± S.D.

CONT = Controls; TRAIN = Combined (Treadmill + Treadmill/Resistance) training group; ACTH = Adrenocorticotrophic hormone; ALDO = Aldosterone; AVP = Vasopressin; K⁺ = Potassium, Na⁺ = Sodium; PROT = Protein; NE = Norepinephrine; EPI = Epinephrine.

Table 4-23. Probabilities for *Type I* Error in Detecting a Change in Hormone Concentration as a Result of 70° Head-up Tilt Before (T1) or After (T3) 6 Months of Exercise Training.

	Group by Time*	Time*	Pre-tilt T1 to Pre-tilt T3†	Tilt T1 to Tilt T3†	Pre-tilt T1 to Tilt T1†	Pre-tilt T3 to Tilt T3†
ACTH	0.05	0.07	0.20	0.07	0.42	0.13
ALDO	0.91	0.08	0.78	0.99	0.03	0.05
AVP	0.14	0.29	0.37	0.16	0.09	0.21
K ⁺	0.69	<0.01	0.10	0.46	<0.01	0.15
Na ⁺	0.81	0.48	0.47	0.31	0.75	0.38
PROT	0.99	<0.01	0.01	<0.01	<0.01	<0.01
NE	0.88	<0.01	0.01	0.34	<0.01	<0.01
EPI	0.59	0.19	0.26	0.72	0.92	0.05

* Wilks' Lambda

† Single-degree-of-freedom contrast, analysis of mean difference

ACTH = Adrenocorticotrophic hormone; ALDO = Aldosterone; AVP = Vasopressin; K⁺ = Potassium, Na⁺ = Sodium; PROT = Protein; NE = Norepinephrine; EPI = Epinephrine.

Means and standard deviations for each hormone/electrolyte analysis are presented in Table 4-22. Values for ACTH are included for reference. The *type I* error rates for detecting a *time X group* interaction and a *time* effect, as well as the error rates associated with detecting a mean difference between two time points are presented in Table 4-23.

In the repeated measures ANOVA for ALDO, the p-value for the *time* effect was 0.08, while the value for the *time X group* interaction was 0.91 (Table 4-23). This suggests that ALDO secretion changed as a result of tilt but was not affected by training. Follow up analyses indicated that changes in resting and tilt concentrations of ALDO from T1 to T3 were due to random variation ($p = 0.78$ and 0.99 for resting and tilt, respectively). However, ALDO increased during tilt at both T1 ($p = 0.03$) and T3 ($p = 0.05$). Aldosterone

increased 20.4% at T1 from an average at rest of $57.3 \pm 30.2 \text{ pg} \cdot \text{ml}^{-1}$ to a tilt average of $69.0 \pm 38.8 \text{ pg} \cdot \text{ml}^{-1}$. Increases at T3 averaged 18.9%, from $59.3 \pm 37.5 \text{ pg} \cdot \text{ml}^{-1}$ at rest to $70.5 \pm 53.6 \text{ pg} \cdot \text{ml}^{-1}$ during tilt (Table 4-22).

An initial analysis for AVP indicated that there was no effect of training on AVP levels ($p = 0.14$ for *time X group* interaction, Table 4-23). In addition, the high *type I* error probability level for a *time* effect ($p = 0.29$) indicated that there was no increase in AVP secretion as a result of tilt at either T1 or T3. Increases during tilt averaged 56% at T1 and 29% at T3 (Table 4-22). However, because these data did not appear normally distributed, a log transformation of the data was made. Analysis of the transformed data indicated that there was an increase in AVP during tilt at T1 ($p = 0.02$); there was no increase at T3 ($p = 0.83$) due to a decrease in AVP secretion by TRAIN ($p < 0.01$).

Changes in resting and tilt plasma Na^+ from T1 to T3 as well as changes in plasma Na^+ during tilt at each test were due to random variation ($p = 0.48$ for overall *time* effect). Changes during tilt at T1 and T3 were less than 1%. Plasma K^+ increased during tilt at T1 ($p < 0.01$) in all groups; the increase averaged $0.2 \text{ mEq} \cdot \text{L}^{-1}$ (4.9%). However, the probability of a *type I* error for detecting a time effect during tilt at T3 was 14.8%, despite the fact that the increase ($0.2 \text{ mEq} \cdot \text{L}^{-1}$, 4.8%) was nearly identical to the T1 change. Changes in resting and tilt plasma K^+ from T1 to T3 were due to random variation ($p = 0.10$ and 0.46 for resting and tilt, respectively).

There was an increase in PROT during tilt at both T1 (9.8%, $p < 0.01$) and T3 (10.5%, $p < 0.01$). In addition, there was an increase in both resting (4.9%, $p = 0.01$) and tilt (5.6%, $p < 0.01$) PROT at T3. These changes were not different between groups ($p = 0.99$ for *time X group* interaction).

Norepinephrine increased during tilt at T1 (50%, $p < 0.01$) and at T3 (86%, $p < 0.01$). Resting NE decreased 26% from T1 to T3 ($p = 0.01$); however, this was not due to training as indicated by the overall *time X group* interaction ($p = 0.88$). The high p -values for a *time* effect and a *time X group* interaction for the EPI response indicate that EPI did not change as a result of either tilt or training.

Responses of Subject Experiencing Presyncopal Symptoms

Four subjects (2 males, 2 females) did not complete the 15 minute tilt portion of the test at T1 ("fainters"). One subject experienced syncope while three others experienced presyncopal symptoms (nausea, sweating, lowered BP) and requested test termination. At T2, three of the original four fainters were able to complete the tilt portion of the test, while at T3 all four subjects successfully completed the 15 minute tilt. Because all of fainters had been assigned to either TREAD ($n = 1$) or TREAD/RESIST ($n = 3$), and since there was an effect of training on the SV and \dot{Q} responses to the tilt test, the cardiovascular responses from these subjects were calculated and compared with those of the 24 subjects in TREAD and TREAD/RESIST who completed the test ("nonfainters"). The HR, SV, \dot{Q} , BP, and TPR responses are listed in Tables 4-24--4-28. For each variable, a 3 X 2 (test X group) repeated measures ANOVA was performed at each time point during the test. However, because of the small number of fainters and the variability of their data, the analyses indicated that differences between fainters and nonfainters at all points for all variables could be ascribed to random variation. Therefore, only descriptive data are offered below.

Table 4-24. Heart Rate Responses of Fainters (F; $n = 4$) and Nonfainters (NF; $n = 24$) to 70° Head-up Tilt Before (T1), After 3 Months (T2), and After 6 Months (T3) of Exercise Training.

Time	T1		T2		T3	
	F	NF	F	NF	F	NF
Rest	59.7± 6.4	65.6±10.6	61.5±11.0	63.4± 8.0	56.9± 6.3	63.0±10.0
T0	70.8±13.4	70.8±14.6	72.5±19.4	69.4±10.5	66.6±10.0	68.4±12.9
T1	71.8±10.6	72.9±12.4	75.6±12.9	72.4± 9.6	69.4±14.2	70.2±11.6
T2	73.6±11.8	73.0±11.7	75.5±14.0	73.0±10.0	70.0±12.2	70.5±11.2
T3	74.2±10.8	72.4±10.8	75.5±13.9	71.6± 8.9	68.9±13.0	70.1±11.4
T4	74.1±12.8	72.4±11.5	77.5±13.2	71.7± 9.0	68.8±10.9	69.7±11.6
T5	71.6± 7.9	72.8±12.5	77.1±14.2	71.4± 9.9	69.5±13.4	69.7±11.5
T6	69.7± 9.6	72.4±11.7	79.0±14.0	72.0± 9.1	69.2±13.0	71.2±12.9
T7	68.4± 7.9	73.4±12.2	76.0±13.9	72.2± 8.9	73.2±14.3	70.9±12.0
T8	73.6±14.6	74.0±12.9	79.8±15.0	72.6± 9.0	69.8±11.9	71.0±12.5
T9	73.0±14.6	74.4±11.9	80.3±16.0	73.7±10.2	73.3±14.8	71.1±12.2
T10	73.3±15.1	74.4±13.7	77.5±15.7	72.3± 9.8	70.3±12.0	71.7±12.9
T11	90.2	75.7±13.3	81.4±10.4	72.8± 9.6	71.6±12.3	72.1±13.4
T12	84.1	76.2±13.7	83.2±14.4	74.5± 9.7	73.4±16.9	73.0±12.3
T13	46.2	75.7±12.3	85.9±13.6	74.0±10.7	70.7±13.0	71.9±13.5
T14	---	76.3±13.8	85.4±15.2	74.9±10.9	70.7±12.4	73.4±13.4
T15	---	76.5±13.6	85.1±12.5	74.6±10.3	71.2±13.8	74.1±13.6
R0	56.2±15.5	71.2±14.1	62.0±15.5	67.3± 8.6	59.6±11.5	67.1±12.4
R1	48.4±11.6	67.6±13.3	60.0±11.8	64.1± 9.4	55.5± 7.0	64.0±10.6
R2	53.6±12.5	65.6±12.9	57.9±11.9	64.3±10.4	51.4± 4.4	62.3±10.4
R3	57.8±12.0	65.7±12.5	56.6±11.6	63.4± 9.5	52.7± 5.3	62.0±10.1
R4	55.7± 9.6	65.4±12.1	58.0±11.4	62.4± 9.3	51.1± 3.2	62.0±10.1
R5	55.9± 7.7	65.2±12.2	58.3±12.8	62.9± 9.7	54.3± 4.8	61.8±10.8
R6	59.0± 8.0	65.4±12.2	59.1±10.8	62.3± 9.7	52.1± 6.1	60.9± 9.3
R7	56.7± 4.8	65.3±11.6	59.5± 9.0	63.6± 9.4	52.0± 4.9	60.9± 9.5
R8	55.5± 5.9	65.6±12.1	58.5±11.2	63.2± 8.9	52.4± 4.5	60.8± 9.6
R9	56.6± 6.3	64.9±11.1	58.4±11.4	62.9± 8.3	53.6± 6.1	60.5± 9.4
R10	58.9± 4.8	65.1±11.1	59.5±11.5	63.0± 8.2	52.8± 3.8	60.4± 9.8
R11	55.5± 5.3	65.2±11.2	58.7±10.3	63.1± 9.0	52.4± 3.4	61.3± 9.5
R12	56.1± 5.2	65.2±10.9	59.9± 9.8	63.3± 8.6	55.3± 8.1	60.6± 8.9
R13	56.4± 5.9	65.4±12.2	58.2±11.6	63.4± 9.3	52.7± 5.1	60.8± 8.9
R14	56.2± 6.0	64.2±10.3	57.3±10.0	63.6± 9.1	54.8± 4.1	61.4± 8.7
R15	55.2± 3.5	64.9±11.8	58.9±11.1	62.9± 8.6	55.5± 7.7	61.6± 8.7

Values are mean ± S.D.

T = Tilt; R = Recovery

Table 4-25. Stroke Volume Responses of Fainters (F; $\underline{n} = 4$) and Nonfainters (NF; $\underline{n} = 24$) to 70° Head-up Tilt Before (T1), After 3 Months (T2), and After 6 Months (T3) of Exercise Training.

Time	T1		T2		T3	
	F	NF	F	NF	F	NF
Rest	43.3± 7.3	47.8±10.1	44.5± 4.2	56.7±10.0	50.7± 4.7	51.9±10.9
T0	30.1± 7.8	37.9± 7.8	33.1± 7.5	40.0± 7.5	36.4± 2.1	39.6± 8.7
T1	30.8± 5.6	36.5± 7.9	30.3± 5.5	37.1± 7.0	36.2± 5.0	38.2± 7.3
T2	31.7± 6.0	36.1± 7.0	29.8± 7.7	37.4± 7.6	33.8± 3.8	37.5± 7.6
T3	32.8± 5.3	36.0± 8.1	31.5± 7.5	38.2± 8.3	37.3± 6.7	37.8± 7.7
T4	31.2± 4.2	36.6± 9.1	29.8± 8.2	38.2± 8.5	36.6± 8.4	38.4± 7.7
T5	33.5± 6.2	36.5± 8.1	29.9± 8.4	38.2± 9.1	36.6± 4.9	37.5± 7.4
T6	36.1± 6.6	36.4± 8.5	32.8± 9.0	38.1± 8.1	37.3± 7.1	37.4± 7.2
T7	36.3± 5.6	36.6± 8.5	31.7± 7.9	38.5± 8.7	36.5± 6.4	37.3± 6.7
T8	32.9± 6.9	37.4±10.0	32.7± 7.8	37.8± 7.9	36.0± 4.7	37.5± 7.5
T9	32.0± 4.7	36.9± 9.7	30.6± 9.3	38.7± 8.6	34.0± 4.8	37.9± 7.7
T10	31.8± 3.1	36.2± 9.4	34.1±11.7	38.9± 8.9	35.7± 5.3	38.2± 9.0
T11	39.0	37.0± 9.5	33.9± 4.7	38.2± 7.0	35.8± 6.0	38.4± 8.6
T12	33.3	35.8± 9.3	32.3± 6.0	36.7± 7.2	33.9± 5.8	37.8± 7.7
T13	44.8	36.1±10.1	34.0± 7.0	38.1± 8.4	35.7± 8.3	39.5± 9.0
T14	---	36.4±10.2	33.7± 8.4	37.2± 8.7	35.6± 5.6	39.0± 9.1
T15	---	35.6±10.6	37.4±11.2	37.4± 8.0	35.5± 6.7	38.1±10.1
R0	50.9± 6.6	47.2±12.6	49.0± 9.4	55.4±13.4	49.0± 4.8	50.8±12.0
R1	50.8± 8.8	49.4±13.0	47.3±12.1	55.2±12.0	47.4± 7.4	52.1±10.8
R2	44.5± 7.3	47.0±12.1	48.2±10.4	54.1±12.8	51.2±12.7	49.7±12.2
R3	47.3±11.4	47.5±13.9	44.9±12.2	54.2±12.6	49.4± 8.3	49.2±12.0
R4	48.7±13.3	45.8±10.8	46.8±11.3	52.1±10.9	49.9± 8.5	48.5±12.3
R5	42.8±13.3	45.6±11.7	47.5±10.7	51.8±11.8	46.7± 6.4	48.6±11.8
R6	44.6± 8.4	45.1±11.8	45.3±12.0	51.5±10.4	51.6± 4.6	49.8±13.3
R7	46.1± 6.6	45.3±12.1	42.7± 5.8	51.0±11.2	49.2± 9.3	48.2±11.7
R8	48.3±10.2	45.7±12.5	44.8± 9.6	51.5±11.9	49.2±10.1	46.7±10.3
R9	49.0± 9.0	45.5±11.4	44.3± 9.0	51.2± 8.9	48.0± 7.5	48.2±12.0
R10	46.5±10.4	45.5±11.4	44.3± 6.7	51.7±10.7	47.6± 5.5	47.6±11.5
R11	48.3±11.2	45.9±12.8	44.7± 7.2	52.9±11.2	47.2± 7.5	47.2±12.8
R12	51.1± 7.3	44.4±10.7	45.9± 6.0	50.6±11.0	47.9± 6.2	48.7±12.2
R13	48.5± 8.9	44.2±12.0	43.7± 6.4	49.9±12.0	49.9± 3.8	49.5±12.3
R14	49.1± 9.8	44.8±13.0	43.4± 8.8	50.1±10.2	49.7± 9.1	50.1±12.7
R15	46.7±10.0	44.0±11.8	43.7± 6.1	50.5± 9.1	48.2±11.0	49.0±13.0

Values are mean ± S.D.

T = Tilt; R = Recovery

Table 4-26. Cardiac Output Responses of Fainters (F; $n = 4$) and Nonfainters (NF; $n = 24$) to 70° Head-up Tilt Before (T1), After 3 Months (T2), and After 6 Months (T3) of Exercise Training.

Time	T1		T2		T3	
	F	NF	F	NF	F	NF
Rest	2.57±0.44	3.10±0.68	2.71±0.35	3.57±0.75	2.89±0.38	3.24±0.83
T0	2.07±0.44	2.62±0.50	2.36±0.57	2.74±0.59	2.43±0.46	2.66±0.55
T1	2.19±0.40	2.62±0.57	2.28±0.50	2.67±0.52	2.54±0.76	2.67±0.47
T2	2.28±0.31	2.59±0.50	2.26±0.70	2.71±0.56	2.38±0.57	2.60±0.50
T3	2.38±0.36	2.57±0.53	2.37±0.62	2.72±0.56	2.59±0.78	2.61±0.51
T4	2.26±0.28	2.62±0.57	2.33±0.79	2.72±0.60	2.53±0.90	2.63±0.47
T5	2.41±0.64	2.61±0.53	2.33±0.79	2.69±0.58	2.57±0.70	2.60±0.51
T6	2.54±0.78	2.58±0.45	2.60±0.88	2.72±0.58	2.65±0.88	2.64±0.49
T7	2.46±0.53	2.62±0.49	2.41±0.69	2.74±0.54	2.71±0.87	2.63±0.47
T8	2.46±0.98	2.73±0.55	2.60±0.76	2.67±0.45	2.54±0.73	2.64±0.47
T9	2.37±0.81	2.68±0.55	2.48±0.89	2.83±0.60	2.53±0.80	2.69±0.48
T10	2.35±0.71	2.63±0.49	2.65±0.98	2.78±0.62	2.55±0.78	2.66±0.44
T11	3.53	2.72±0.46	2.75±0.41	2.76±0.53	2.61±0.82	2.69±0.46
T12	2.79	2.66±0.49	2.66±0.56	2.72±0.52	2.51±0.85	2.70±0.44
T13	2.07	2.66±0.50	2.91±0.69	2.79±0.59	2.58±1.00	2.76±0.57
T14	—	2.70±0.49	2.87±0.92	2.75±0.56	2.53±0.73	2.76±0.45
T15	—	2.63±0.47	2.78±0.45	2.75±0.53	2.56±0.82	2.72±0.46
R0	2.86±0.84	3.28±0.78	3.04±0.84	3.72±0.86	2.96±0.86	3.34±0.87
R1	2.51±0.94	3.22±0.76	2.81±0.70	3.50±0.71	2.67±0.76	3.33±0.72
R2	2.39±0.70	2.99±0.61	2.76±0.60	3.41±0.76	2.63±0.67	3.09±0.61
R3	2.63±0.82	3.03±0.72	2.51±0.66	3.37±0.68	2.62±0.61	2.96±0.63
R4	2.47±0.57	2.94±0.69	2.69±0.63	3.21±0.63	2.61±0.52	2.93±0.66
R5	2.20±0.55	2.91±0.68	2.70±0.40	3.21±0.68	2.56±0.56	2.93±0.67
R6	2.64±0.62	2.87±0.62	2.64±0.58	3.20±0.65	2.69±0.42	2.96±0.74
R7	2.61±0.44	2.89±0.69	2.53±0.48	3.21±0.69	2.54±0.54	2.87±0.73
R8	2.66±0.41	2.94±0.71	2.59±0.53	3.17±0.71	2.57±0.53	2.79±0.66
R9	2.66±0.59	2.90±0.67	2.57±0.54	3.19±0.55	2.59±0.63	2.84±0.72
R10	2.78±0.72	2.89±0.64	2.62±0.47	3.24±0.73	2.52±0.46	2.83±0.71
R11	2.82±0.75	2.92±0.67	2.61±0.48	3.32±0.76	2.49±0.52	2.82±0.74
R12	2.88±0.55	2.86±0.70	2.67±0.59	3.17±0.66	2.65±0.49	2.91±0.76
R13	2.66±0.56	2.84±0.75	2.52±0.48	3.12±0.67	2.64±0.38	2.95±0.70
R14	2.75±0.61	2.82±0.70	2.47±0.51	3.15±0.63	2.73±0.62	3.02±0.77
R15	2.67±0.59	2.81±0.69	2.56±0.54	3.17±0.61	2.70±0.74	2.95±0.74

Values are mean ± S.D.

T = Tilt; R = Recovery

Table 4-27. Systolic and Diastolic Blood Pressure Responses of Fainters (F; $n = 4$) and Nonfainters (NF; $n = 24$) to 70° Head-up Tilt Before (T1), After 3 Months (T2), and After 6 Months (T3) of Exercise Training.

Time	T1		T2		T3	
	F	NF	F	NF	F	NF
SBP (mmHg)						
Rest	125 ± 19	125 ± 11	131 ± 18	127 ± 14	126 ± 14	131 ± 18
T0	131 ± 23	123 ± 13	131 ± 17	117 ± 18	131 ± 18	127 ± 21
T1	140 ± 37	125 ± 13	134 ± 12	122 ± 16	125 ± 16	127 ± 22
T2	134 ± 20	125 ± 12	133 ± 13	120 ± 17	134 ± 15	130 ± 22
T3	132 ± 20	125 ± 13	139 ± 13	122 ± 15	133 ± 13	133 ± 22
T4	130 ± 20	124 ± 12	135 ± 16	121 ± 15	139 ± 13	130 ± 15
T5	134 ± 22	126 ± 14	137 ± 16	121 ± 18	135 ± 15	131 ± 19
T10	131 ± 27	126 ± 12	132 ± 25	124 ± 16	130 ± 15	133 ± 22
T15	—	123 ± 14	138 ± 24	123 ± 16	136 ± 4	130 ± 22
R0	111 ± 11	125 ± 16	129 ± 13	126 ± 12	133 ± 6	133 ± 15
R1	117 ± 18	124 ± 13	130 ± 16	129 ± 13	128 ± 21	133 ± 16
R2	119 ± 19	124 ± 14	132 ± 15	127 ± 15	132 ± 16	132 ± 17
R3	120 ± 21	124 ± 12	133 ± 16	128 ± 13	138 ± 11	133 ± 17
R4	124 ± 24	125 ± 13	130 ± 15	126 ± 12	135 ± 10	133 ± 18
R5	126 ± 26	125 ± 13	129 ± 22	126 ± 14	125 ± 21	132 ± 18
R10	126 ± 21	125 ± 12	131 ± 26	126 ± 15	127 ± 17	131 ± 22
R15	125 ± 21	123 ± 12	134 ± 20	127 ± 16	129 ± 16	130 ± 19
DBP (mmHg)						
Rest	79 ± 7	78 ± 5	78 ± 8	77 ± 5	77 ± 4	76 ± 6
T0	84 ± 9	80 ± 6	86 ± 6	79 ± 11	80 ± 10	81 ± 11
T1	87 ± 13	81 ± 7	87 ± 7	81 ± 8	79 ± 8	81 ± 10
T2	84 ± 8	82 ± 6	88 ± 7	81 ± 8	85 ± 6	81 ± 8
T3	85 ± 9	82 ± 6	88 ± 6	81 ± 8	84 ± 6	82 ± 8
T4	82 ± 10	83 ± 6	88 ± 5	79 ± 8	84 ± 8	82 ± 9
T5	85 ± 12	83 ± 7	87 ± 4	81 ± 9	84 ± 5	81 ± 9
T10	84 ± 20	84 ± 7	84 ± 11	81 ± 7	83 ± 6	81 ± 9
T15	—	81 ± 6	87 ± 8	80 ± 8	84 ± 6	82 ± 8
R0	74 ± 9	78 ± 7	80 ± 6	78 ± 7	80 ± 2	77 ± 6
R1	78 ± 9	79 ± 6	81 ± 9	78 ± 6	75 ± 7	77 ± 6
R2	78 ± 9	80 ± 6	82 ± 7	79 ± 5	76 ± 6	78 ± 5
R3	78 ± 11	79 ± 6	80 ± 10	78 ± 6	79 ± 4	78 ± 6
R4	79 ± 12	80 ± 6	81 ± 11	79 ± 6	78 ± 3	78 ± 7
R5	78 ± 11	79 ± 6	81 ± 12	79 ± 6	76 ± 6	78 ± 7
R10	76 ± 9	79 ± 5	82 ± 10	78 ± 6	78 ± 6	78 ± 6
R15	76 ± 10	79 ± 6	81 ± 11	79 ± 6	77 ± 5	78 ± 6

Values are mean ± S.D.

T = Tilt; R = Recovery

Table 4-28. Mean Arterial Blood Pressure and Total Peripheral Resistance Responses of Fainters (F; \bar{n} = 4) and Nonfainters (NF; \bar{n} = 24) to 70° Head-up Tilt Before (T1), After 3 Months (T2), and After 6 Months (T3) of Exercise Training.

Time	T1		T2		T3	
	F	NF	F	NF	F	NF
MAP (mmHg)						
Rest	94 ± 11	93 ± 6	96 ± 11	94 ± 7	93 ± 7	94 ± 9
T0	99 ± 13	94 ± 6	100 ± 10	92 ± 11	97 ± 12	96 ± 12
T1	105 ± 21	95 ± 7	103 ± 9	94 ± 9	94 ± 11	96 ± 13
T2	100 ± 12	96 ± 7	103 ± 9	93 ± 10	101 ± 9	97 ± 12
T3	100 ± 12	96 ± 7	104 ± 8	94 ± 9	100 ± 8	98 ± 11
T4	98 ± 13	97 ± 7	104 ± 8	93 ± 9	102 ± 9	98 ± 10
T5	101 ± 15	97 ± 8	103 ± 8	94 ± 11	100 ± 8	98 ± 10
T10	100 ± 22	98 ± 7	100 ± 15	95 ± 9	96 ± 8	98 ± 11
T15	—	95 ± 8	104 ± 13	94 ± 10	101 ± 3	98 ± 11
R0	86 ± 10	94 ± 9	96 ± 9	94 ± 7	98 ± 1	96 ± 8
R1	91 ± 12	94 ± 8	97 ± 11	95 ± 7	92 ± 12	96 ± 7
R2	91 ± 12	94 ± 8	98 ± 10	95 ± 7	95 ± 9	96 ± 8
R3	92 ± 14	94 ± 7	98 ± 12	95 ± 6	98 ± 6	96 ± 8
R4	93 ± 16	95 ± 8	97 ± 12	95 ± 6	97 ± 5	96 ± 9
R5	93 ± 15	94 ± 7	97 ± 14	94 ± 7	92 ± 11	96 ± 9
R10	92 ± 13	94 ± 7	98 ± 15	94 ± 8	94 ± 9	95 ± 9
R15	92 ± 14	94 ± 7	99 ± 14	95 ± 8	94 ± 8	95 ± 9
TPR (dyne sec•cm ⁻⁵)						
Rest	3030± 863	2518±535	2866± 566	2214±592	2649± 503	2467±651
T0	3947± 867	2987±566	3538± 811	2759±648	3227± 453	2979±705
T1	3434± 151	3067±672	3677± 532	2935±689	3119± 779	2939±683
T2	3528± 281	3089±658	3947±1350	2875±688	3500± 720	3001±679
T3	3397± 294	3112±676	3721±1046	2905±722	3245± 733	3089±617
T4	3484± 474	3110±663	3889±1435	2809±622	3517±1209	3042±632
T5	3277± 755	3084±634	3873±1368	2925±741	3290± 851	3095±717
T10	3428± 278	3069±597	3311±1120	2873±758	3281± 907	2965±533
T15	—	3006±618	2994± 281	2837±660	3426±1318	2812±535
R0	2570± 828	2386±536	2729±1011	2137±642	2776± 740	2423±656
R1	3188±1208	2456±610	2931± 922	2296±740	3087± 872	2371±462
R2	3254±1059	2611±519	2979± 806	2366±745	3063± 991	2569±582
R3	3132± 842	2655±708	3308±1095	2368±733	3343± 923	2677±582
R4	3109± 913	2695±599	3034± 910	2454±574	3038± 726	2727±623
R5	3551±1202	2724±655	2924± 622	2467±682	3016± 841	2711±604
R10	2752± 627	2730±619	3090± 845	2444±658	3070± 654	2825±793
R15	2496± 262	2852±829	3192± 840	2491±627	2986± 960	2696±721

Values are mean ± S.D.; T = Tilt; R = Recovery

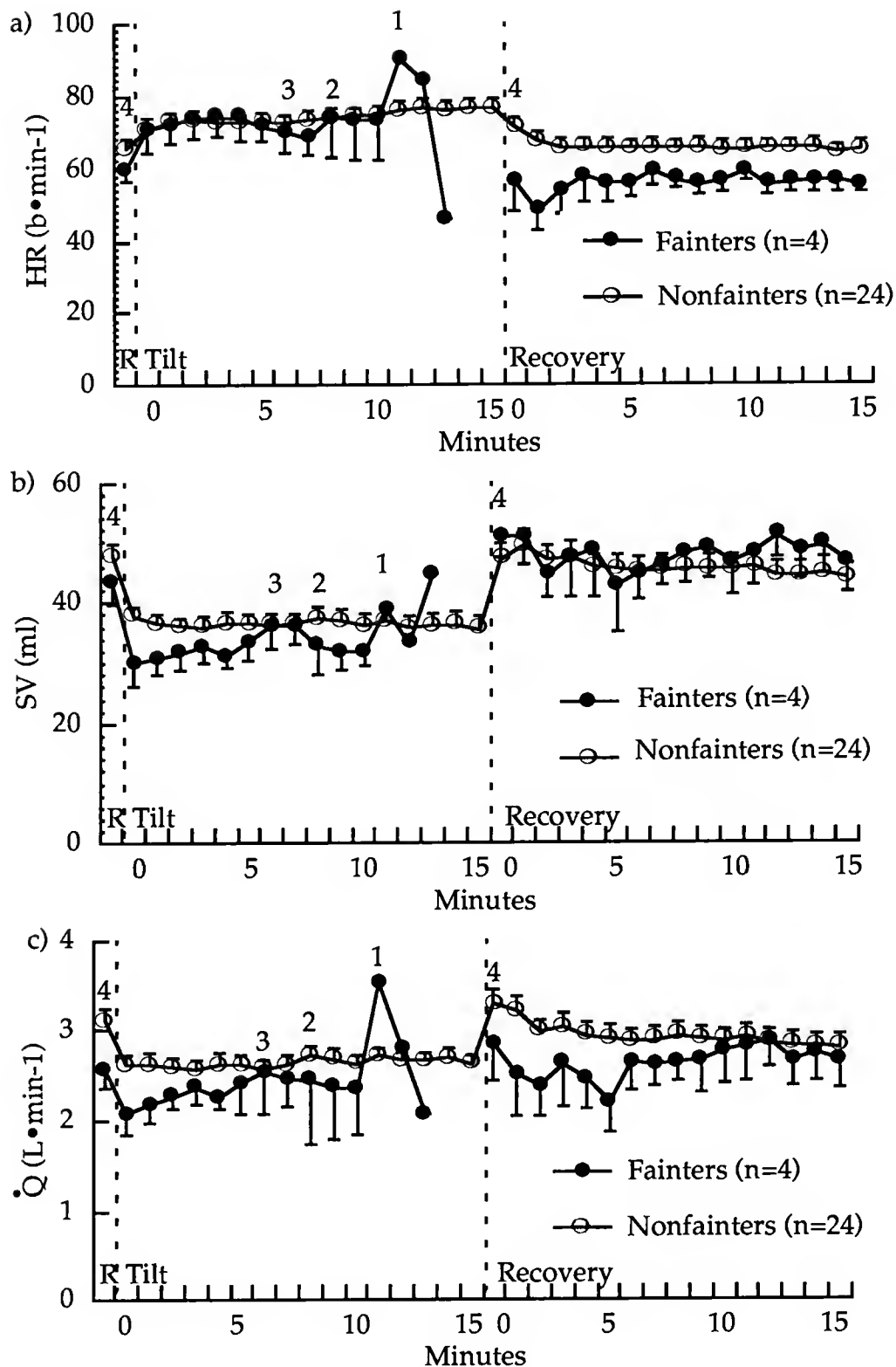


Figure 4-3. Responses of fainters vs. nonfainters to 70° head-up tilt prior to exercise training: a) heart rate (HR); b) stroke volume (SV); c) cardiac output (\dot{Q}). (R = Rest; Numbers above data points are number of fainters used in calculation of means at all times up to next marked point.)

The HR responses of the two groups at T1 are shown in Figure 4-3. The numbers above the time points in the graph represent the number of fainters used in calculating that mean and all subsequent means prior to the next marked point. Thus, all four fainters were used in calculating the means at rest and through TILT₅; three fainters were used for calculations for TILT₆ and TILT₇. Two fainters were represented at TILT₈ through TILT₁₀, while one fainter was used at TILT₁₁ through TILT₁₃. All four fainters were used in calculation of REC data.

The HR responses of the fainters appear nearly identical to those of the nonfainters through TILT₁₀. The response after minute 10 (one subject) shows a sharp increase, followed by a precipitous drop. The REC₀ and REC₁ HRs for the fainters were approximately 12-13 b•min⁻¹ below that of the nonfainters. HR for the fainters remained approximately 6-8 b•min⁻¹ below that of the nonfainters throughout the remainder of REC.

The resting SV of the fainters at T1 was approximately 5 ml below that of the nonfainters (Figure 4-3). Although the response during TILT was erratic, at most time points through TILT₁₀ the SV remained approximately 5 ml below that of nonfainters. The response after minute 10 (one subject) shows an erratic pattern with a tendency to be elevated above the nonfainters' response. Stroke volume during REC continued an irregular pattern but appeared similar to the nonfainters' response throughout most REC.

The \dot{Q} response of the fainters at T1 was approximately 0.50 L•min⁻¹ lower than that of nonfainters at rest (Figure 4-3). The erratic pattern during tilt mirrored that of the SV response. The response after minute 10 (one subject) showed a large increase prior to a precipitous drop. Cardiac output during REC was initially depressed between 0.33 and 0.68 L•min⁻¹ through REC₅. It recovered somewhat between REC₆ and REC₉ and was only

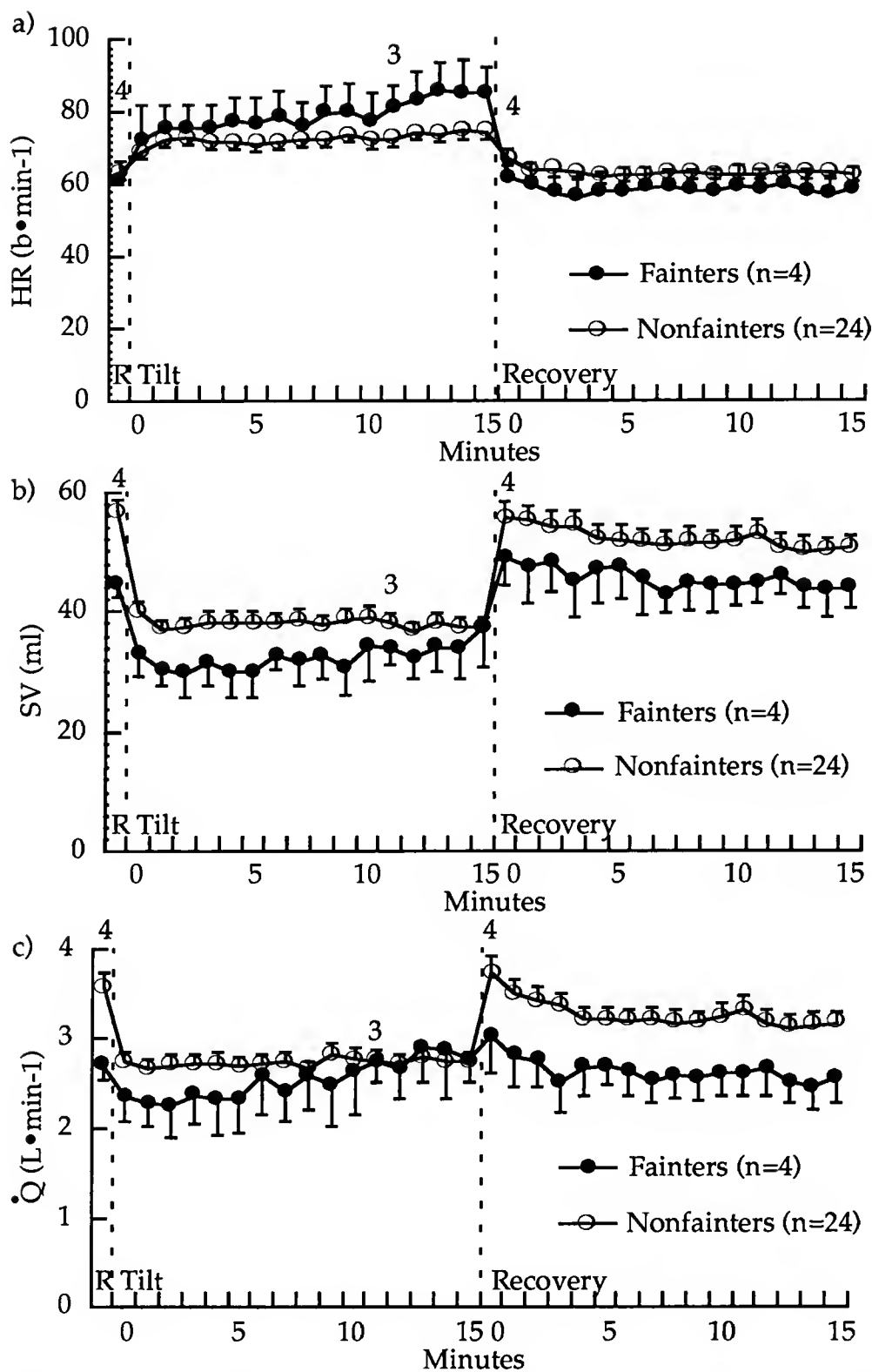


Figure 4-4. Responses of fainters vs. nonfainters to 70° head-up tilt after 3 months of exercise training: a) heart rate (HR); b) stroke volume (SV); c) cardiac output (\dot{Q}). (R = Rest; Numbers above data points are number of fainters used in calculation of means at all times up to next marked point.)

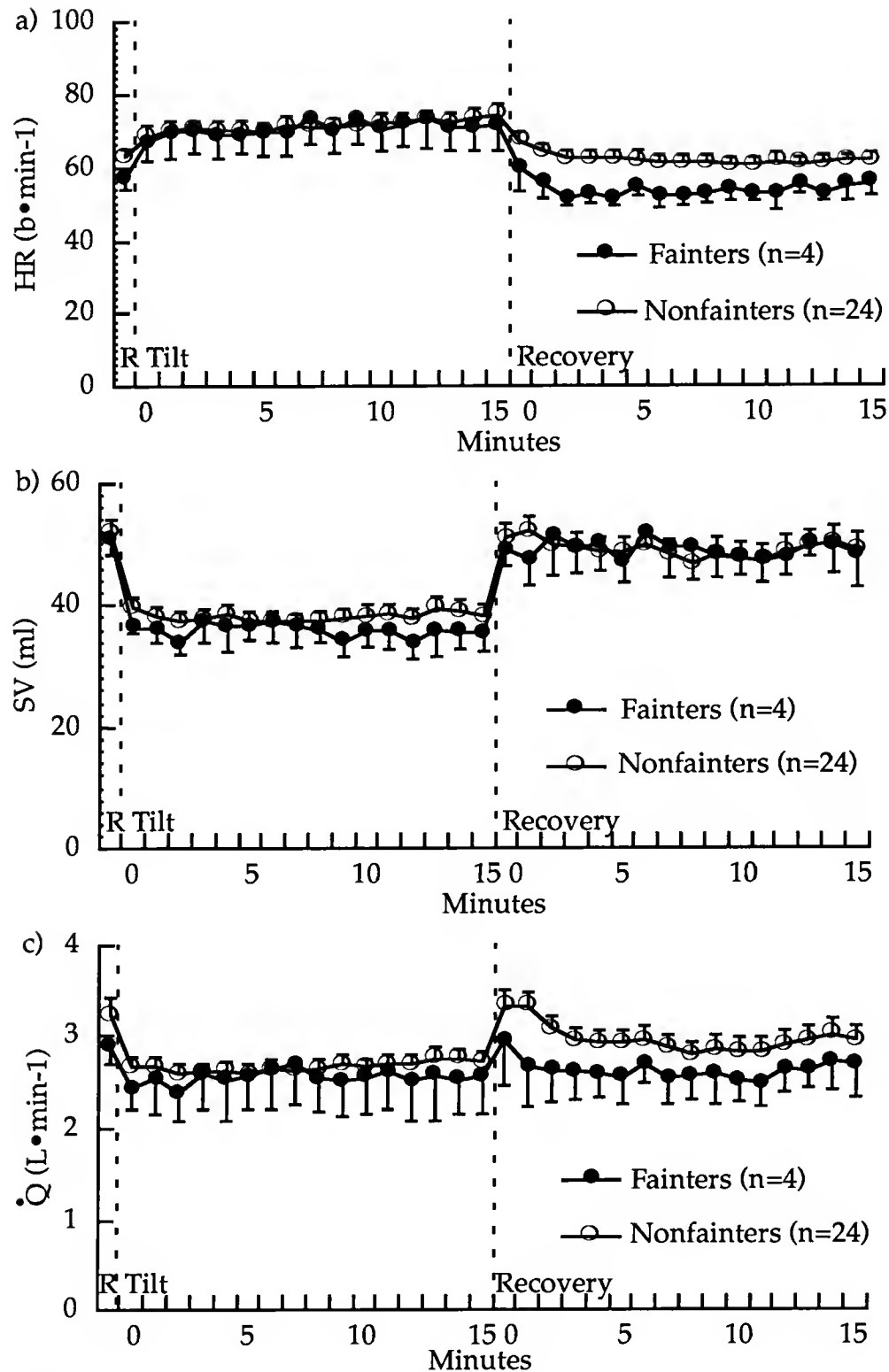


Figure 4-5. Responses of fainters vs. nonfainters to 70° head-up tilt after 6 months of exercise training: a) heart rate (HR); b) stroke volume (SV); c) cardiac output (\dot{Q}). (R = Rest; All four fainters used in calculation of means at all time points.)

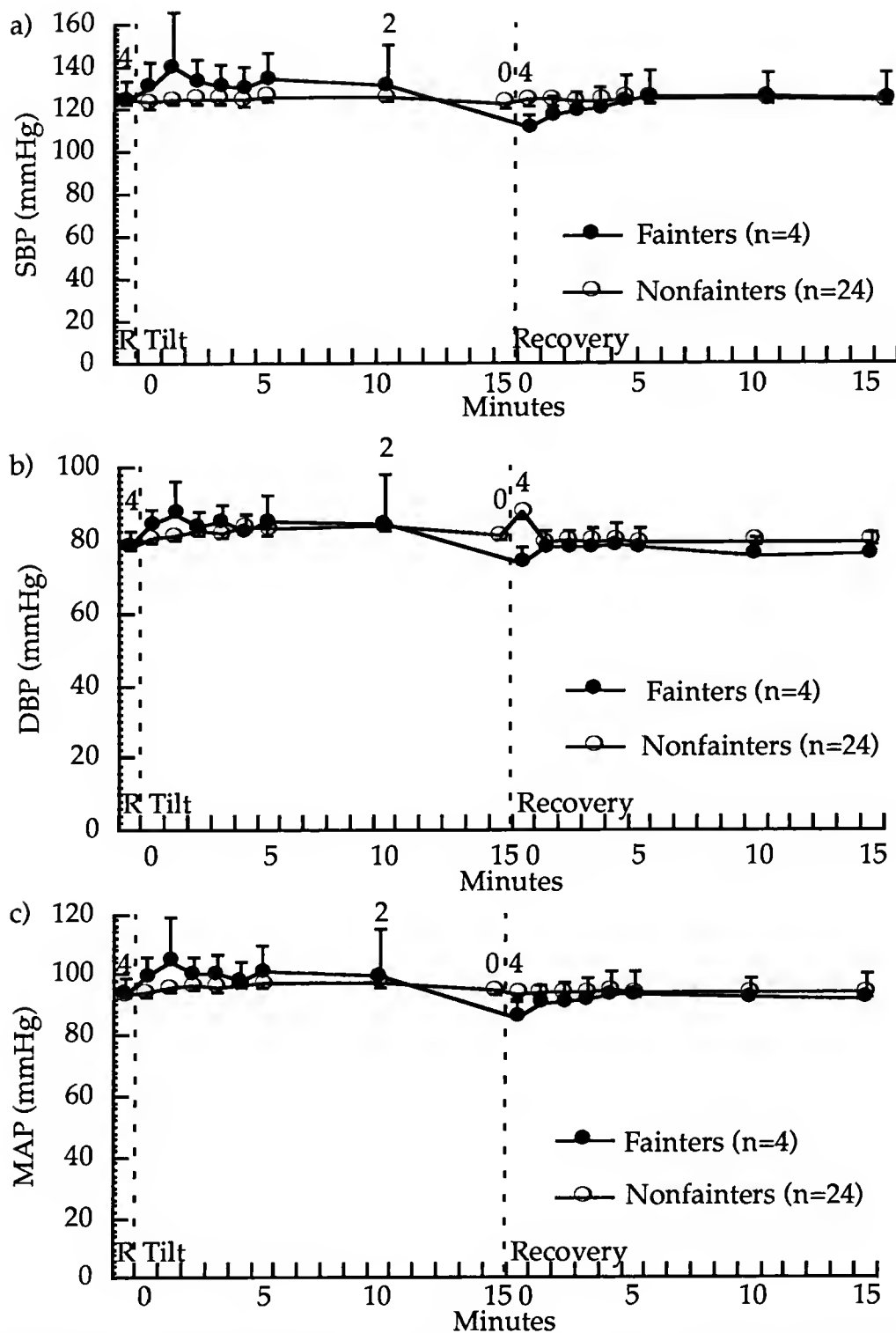


Figure 4-6. Responses of fainters vs. nonfainters to 70° head-up tilt before exercise training: a) systolic blood pressure (SBP); b) diastolic blood pressure (DBP); c) mean arterial pressure (MAP). (R = Rest; Numbers above data points are number of fainted individuals used in calculation of means at all times up to next marked point.)

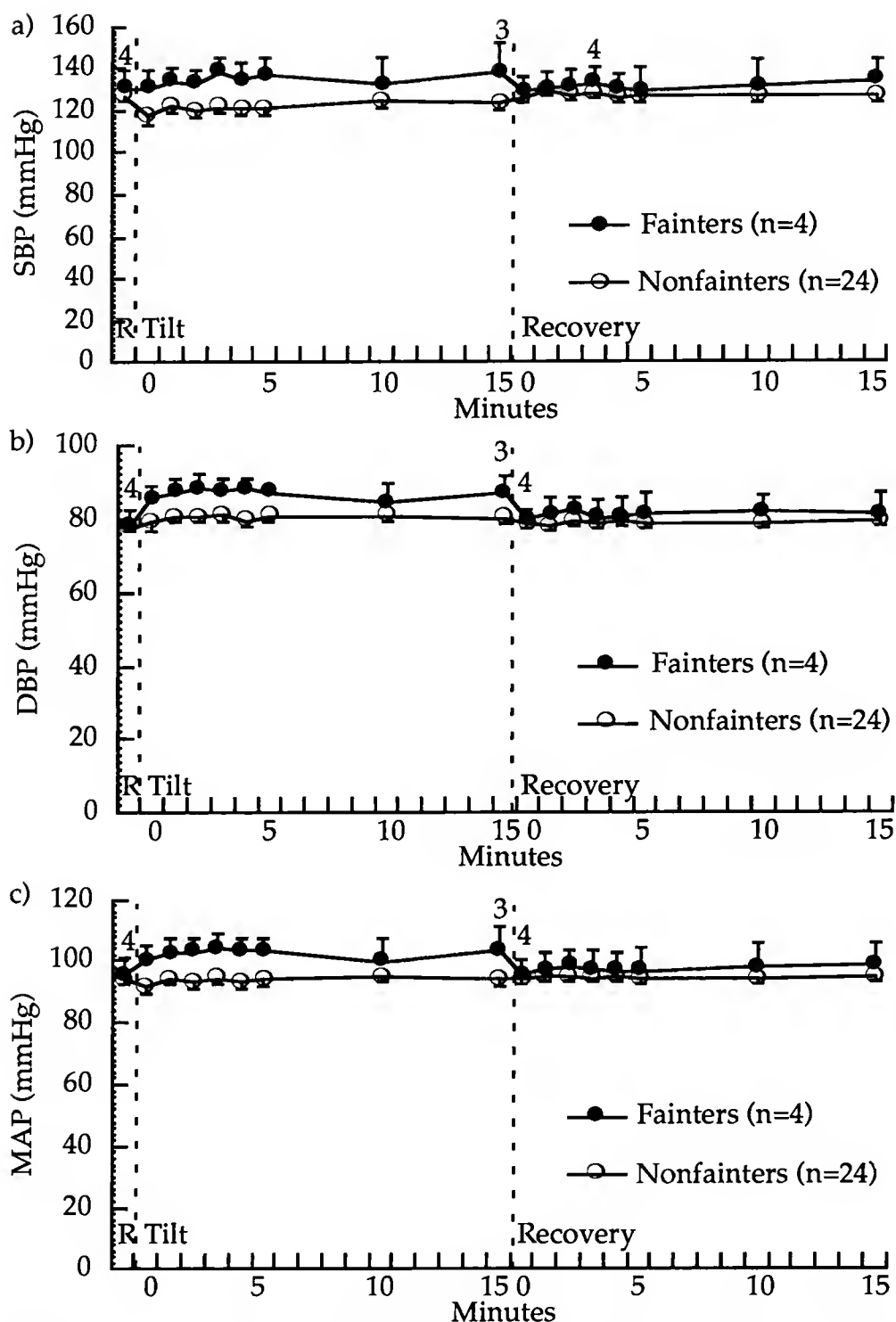


Figure 4-7. Responses of fainters vs. nonfainters to 70° head-up tilt after 3 months of exercise training: a) systolic blood pressure (SBP); b) diastolic blood pressure (DBP); c) mean arterial pressure (MAP). (R = Rest; Numbers above data points are number of fainters used in calculation of means at all times up to next marked point.)

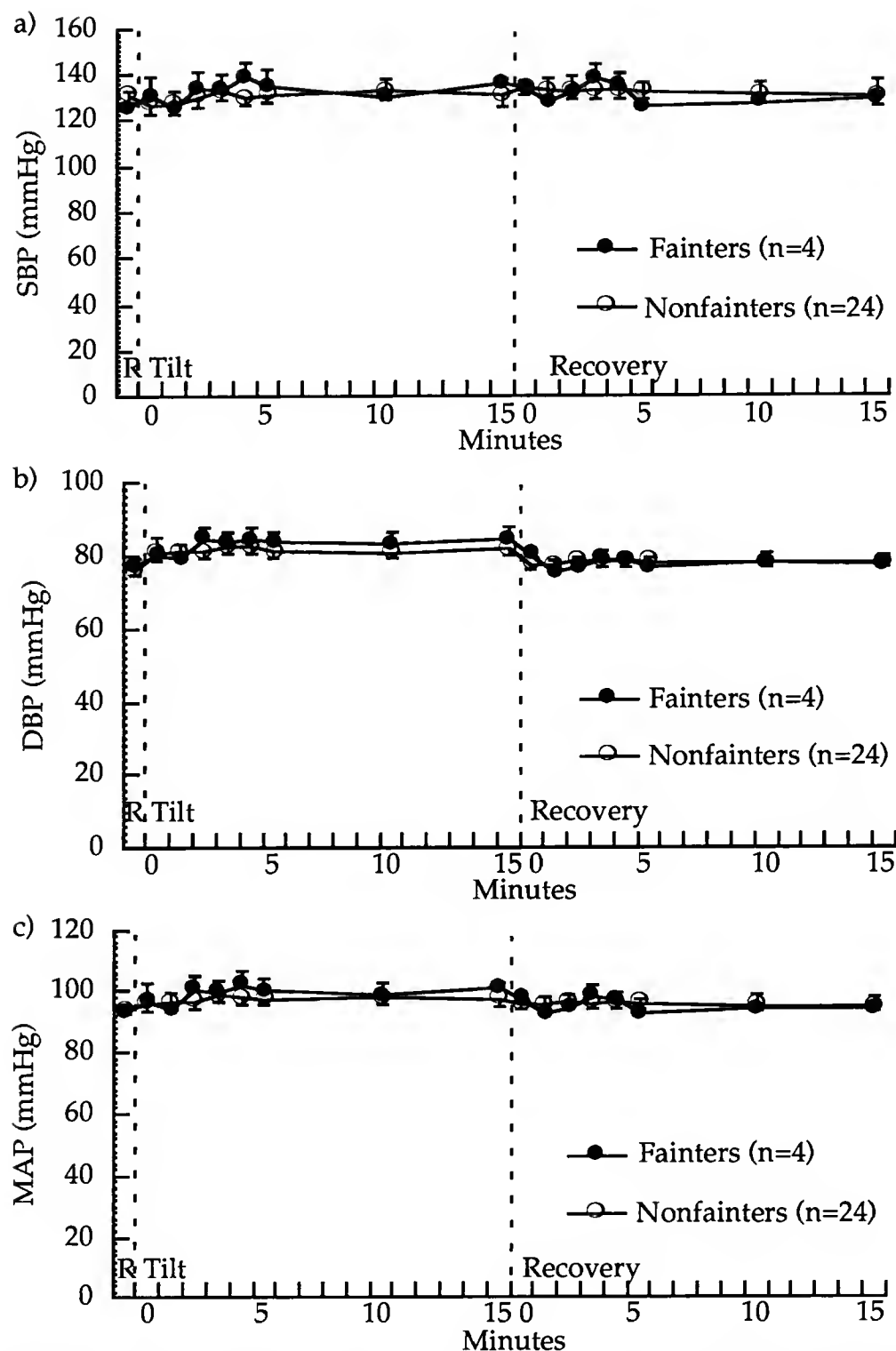


Figure 4-8. Responses of fainters vs. nonfainters to 70° head-up tilt after 6 months of exercise training: a) systolic blood pressure (SBP); b) diastolic blood pressure (DBP); c) mean arterial pressure (MAP). (R = Rest; All four fainters used in calculation of means at all time points.)

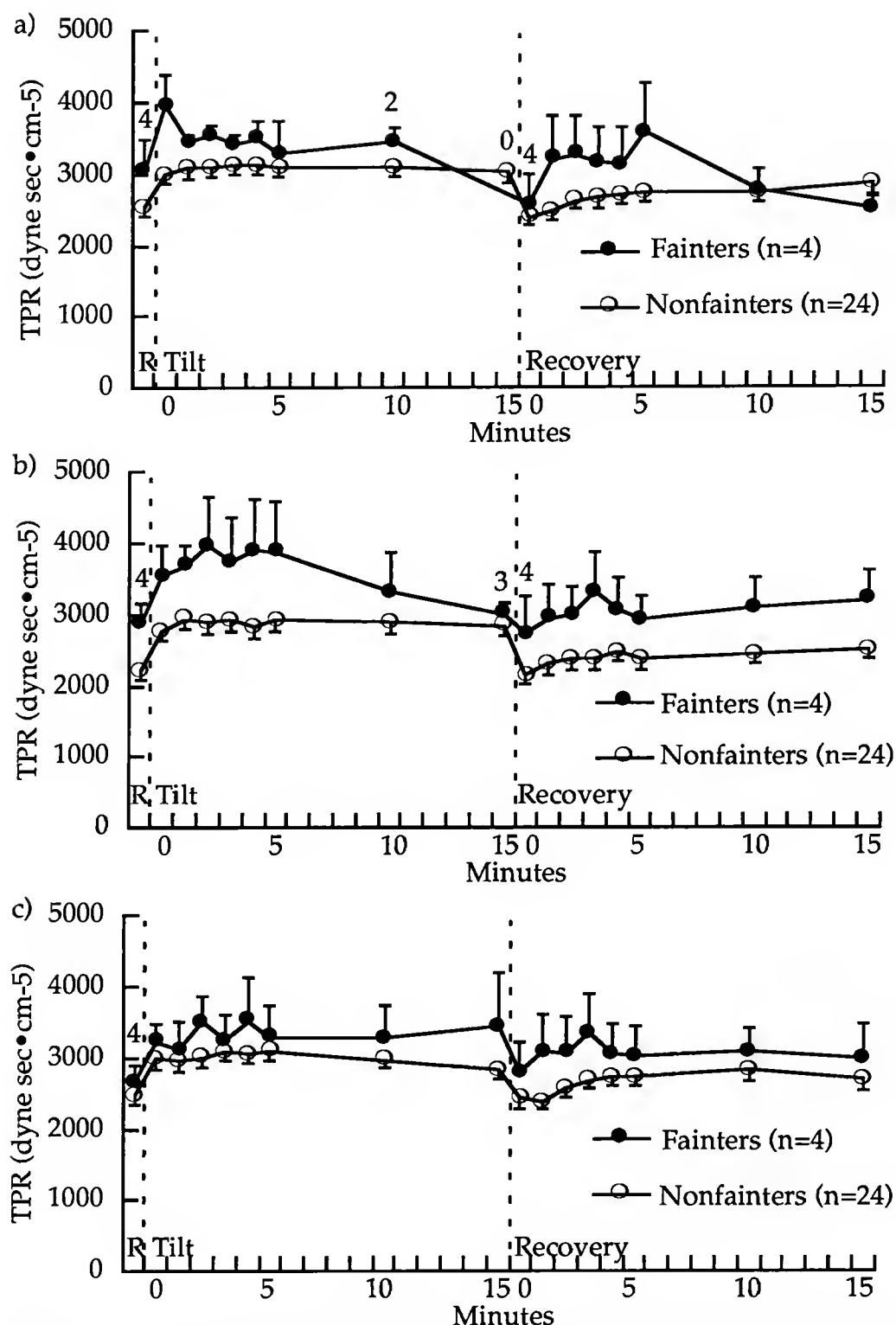


Figure 4-9. Total peripheral resistance response of fainters vs. nonfainters to 70° head-up tilt: a) before exercise training; b) after 3 months of exercise training; c) after 6 months of exercise training. (R = Rest; Numbers above data points are number of fainters used in calculation of means at all times up to next marked point.)

depressed 0.21 to $0.28 \text{ L} \cdot \text{min}^{-1}$ below that of nonfainters. Differences between nonfainters and fainters were negligible after that point.

Three of the four subjects who were unable to complete the tilt portion of the test at T1 were able complete the tilt at T2. The HR, SV, and \dot{Q} comparisons at T2 of these subjects and the 24 nonfainters are shown in Figure 4-4. At rest, the HR response is nearly equal. However, in contrast to T1, the HR response of the fainters shows a steady increase throughout TILT and is approximately $10\text{-}11 \text{ b} \cdot \text{min}^{-1}$ higher than nonfainters toward the end of TILT. The HR of fainters is slightly below that of nonfainters throughout REC.

The SV response of the fainters is consistently below that of the nonfainters throughout rest, TILT and REC. The \dot{Q} response, while initially depressed, approximates that of the nonfainters toward the end of TILT in response to the higher HR. The \dot{Q} of fainters during REC is consistently depressed between 0.51 and $0.86 \text{ L} \cdot \text{min}^{-1}$ when compared to the nonfainters' response.

The T3 HR, SV, and \dot{Q} comparisons between the two groups are shown in Figure 4-5. The HR response of the two groups during TILT is nearly identical; however, the response of the fainters during REC is still somewhat lower. The SV response of the two groups is nearly identical throughout the entire test, reflecting predominantly an increased response by the fainters. The \dot{Q} responses during TILT are similar, reflecting slight increases by the fainters and slight decreases by the nonfainters. During REC, the response of the fainters is still below that of the nonfainters but by a smaller margin than at T2.

At T1, fainters had similar BP responses to nonfainters during supine rest prior to tilt (Tables 4-27--4-28; figure 4-6). However, at the initiation of tilt,

fainters had increases of 6 and 5 mmHg in SBP and DBP, respectively, while nonfainters showed a 2 mmHg decrease in SBP and a 2 mmHg increase in DBP. During tilt prior to the onset of symptoms, the SBP of fainters was 6 to 15 mmHg higher than that of nonfainters, while the DBP was up to 6 mmHg higher. The SBP for fainters at REC₀ was 14 mmHg below that of the nonfainters, but gradually recovered by REC₄. The DBP for fainters at REC₀ was 4 mmHg below that of nonfainters but recovered by REC₁.

At T2, the BP responses of the fainters were consistently higher than those of nonfainters (Tables 4-27--4-28; Figure 4-7). This appears to be due to both a decrease in the nonfainters' response and an increase in the fainters' response. The fainters' response may be due to apprehension regarding the test. At T3, the responses of fainters and nonfainters appear similar.

Total peripheral resistance responses are shown in Table 4-28 and Figure 4-9. Fainters had higher resting TPR values, reflective of a lower \dot{Q} (Table 4-26). The greater TPR values during tilt for fainters at T1 and at T2 were associated with generally higher MAP and the generally lower \dot{Q} . TPR values for the two groups are more similar during tilt at T3. The absolute and percentage change data for HR, SV, \dot{Q} , SBP, DBP, MAP, and TPR at T1, T2, and T3 are presented for each fainter in Appendix E.

Initial characteristics of the fainters and nonfainters are listed in Table 4-29. Sample sizes for the nonfainters are as listed earlier under each respective analysis section. Analyses (one-way ANOVA) of differences between the fainters and nonfainters at T1 for each characteristic or test showed that any group differences could be ascribed to random variation (Table 4-29). However, the small number of fainters limits the power of the analyses. Even so, a visual inspection of the data shows no obvious differences between the two groups that could help explain the lack of initial

Table 4-29. Comparison of Subject Characteristics, Aerobic Capacity, Strength, and Body Composition of Nonfainters ($\underline{n} = 24$) vs. Fainters ($\underline{n} = 4$) Prior to Exercise Training.

	Nonfainters	Fainters	p
Age (yrs)	69.5 \pm 5.6	70.3 \pm 6.5	0.82
Height (cm)	164.6 \pm 9.1	168.4 \pm 11.7	0.47
Weight (kg)	67.8 \pm 15.5	75.3 \pm 7.6	0.31
$\dot{V}O_2\text{max}$ (ml \cdot kg ⁻¹ \cdot min ⁻¹)	23.0 \pm 4.4	23.0 \pm 7.2	0.97
Strength			
Leg press (kg)	155.8 \pm 103.9	175.0 \pm 75.2	0.62
Biceps curl (kg)	44.8 \pm 21.9	47.5 \pm 17.7	0.82
Triceps extension (kg)	34.6 \pm 14.8	40.0 \pm 12.7	0.49
Lumbar extension (Nm)	936 \pm 521	954 \pm 431	0.98
Body Composition			
Sum of 7 skinfolds (mm)	168.3 \pm 61.4	197.0 \pm 87.2	0.41
Lean mass (kg)	41.1 \pm 11.4	44.3 \pm 8.5	0.59
Lower body lean mass (kg)	14.1 \pm 3.8	15.5 \pm 3.8	0.48

Values are mean \pm S.D.

tolerance of the fainters for the tilt test. Differences between the two groups in age, height, and weight were not striking. Initial aerobic power measurements of the two groups were nearly identical. Fainters were somewhat stronger than nonfainters, particularly in the LP. In body composition measures, fainters had greater lean mass than nonfainters; however, when lean mass and lower body lean mass were calculated as a percentage of total mass and lower body mass, respectively, the groups were nearly equal. Lean mass as a percentage of total mass was 63.7% and 61.3% for nonfainters and fainters, respectively, while lower body lean mass as a percentage of lower body mass was 60.4% and 59.9% for nonfainters and fainters, respectively. Although it appeared that fainters tended to have a

larger $\Sigma 7$ skinfold measurement, these data were somewhat skewed since one subject in the fainters group had one of the largest measurements.

Measurements of blood volume variables and hormone concentrations at rest and in response to tilt are listed for nonfainters and fainters in Table 4-30. Sample size for the nonfainters is $\underline{n} = 18$ for plasma and blood volume and $\underline{n} = 27$ for hormone analyses. Blood volume was measured successfully in only two of the fainters, while hormone concentrations were measured in three of the fainters. Although statistical comparisons between the two groups were made, the small sample size for the fainters limits the power of the analyses. Therefore, primarily qualitative observations will be made.

Fainters appeared to have a slightly higher PV than nonfainters at T1 but a greater decline during tilt (720 ml, 24.6% vs. 564 ml, 20.8%). This is despite the fact that the fainters were tilted for a shorter time interval than the nonfainters. Both groups had smaller absolute and relative declines at T3: 642 ml, 20.0% for fainters and 525 ml 18.4% for nonfainters.

Fainters had larger relative increases in ALDO during tilt: at T1, ALDO increased 94.5% in the fainters while the increase in nonfainters was 20.4%. This disparity remained at T3, when all of the fainters were able to complete the tilt portion of the test. Fainters had a greater baseline PROT concentration at T1; however, while the PROT concentration of the fainters decreased 4.4% from T1 to T3, that of the nonfainters increased by 4.9%.

A striking difference between the two groups was in the AVP and ACTH responses to tilt (Figure 4-10). Nonfainters had a 56% increase in AVP as a result of tilt. Fainters, on the other hand, had a 1526% increase despite a shorter tilt interval. After 6 months of training, fainters still had a large relative increase in AVP (1258%), although the absolute resting and tilt

Table 4-30. Comparison of Blood Volume and Hormone Responses of Nonfainters ($\underline{n} = 24$) vs. Fainters ($\underline{n} = 4$) to 70° Head-up Tilt Before and After 6 Months of Exercise Training.

	Pre-training		Post-training	
	Rest	Tilt	Rest	Tilt
PV (ml)				
Nonfainters ($\underline{n} = 18$)	2715 \pm 668	2151 \pm 491	2853 \pm 867	2328 \pm 821
Fainters ($\underline{n} = 2$)	2928 \pm 339	2208 \pm 182	3202 \pm 687	2560 \pm 528
BV (ml)				
Nonfainters ($\underline{n} = 18$)	4130 \pm 1077	3647 \pm 878	4394 \pm 1399	4027 \pm 1423
Fainters ($\underline{n} = 2$)	3994 \pm 215	3657 \pm 430	4746 \pm 1076	4421 \pm 1116
RCV (ml)				
Nonfainters ($\underline{n} = 18$)	1415 \pm 429	1496 \pm 415	1541 \pm 550	1699 \pm 634
Fainters ($\underline{n} = 2$)	1466 \pm 441	1449 \pm 247	1544 \pm 389	1861 \pm 588
ACTH (pg•ml ⁻¹)				
Nonfainters ($\underline{n} = 27$)	50.2 \pm 30.0	52.8 \pm 40.0	57.0 \pm 35.7	61.0 \pm 38.2
Fainters ($\underline{n} = 3$)	51.8 \pm 18.3	183.4 \pm 173.1	49.1 \pm 28.8	148.4 \pm 149.5
ALDO (pg•ml ⁻¹)				
Nonfainters ($\underline{n} = 27$)	57.3 \pm 30.2	69.0 \pm 38.8	59.3 \pm 37.5	70.5 \pm 53.6
Fainters ($\underline{n} = 3$)	43.7 \pm 5.3	85.0 \pm 25.6	51.9 \pm 42.9	97.0 \pm 22.9
AVP (pg•ml ⁻¹)				
Nonfainters ($\underline{n} = 27$)	2.5 \pm 2.8	3.9 \pm 3.8	1.7 \pm 1.4	2.2 \pm 2.6
Fainters ($\underline{n} = 3$)	3.9 \pm 2.7	63.4 \pm 39.0	1.2 \pm 0.4	16.3 \pm 11.4
K ⁺ (mEq•L ⁻¹)				
Nonfainters ($\underline{n} = 17$)	4.1 \pm 0.3	4.3 \pm 0.3	4.2 \pm 0.4	4.4 \pm 0.3
Fainters ($\underline{n} = 3$)	4.1 \pm 0.2	4.3 \pm 0.2	4.1 \pm 0.2	4.5 \pm 0.2
Na ⁺ (mEq•L ⁻¹)				
Nonfainters ($\underline{n} = 27$)	140.4 \pm 2.0	140.7 \pm 2.9	141.1 \pm 3.2	141.5 \pm 2.8
Fainters ($\underline{n} = 3$)	141.2 \pm 0.3	140.8 \pm 0.6	141.2 \pm 0.4	142.6 \pm 1.3
PROT (mg•dl ⁻¹)				
Nonfainters ($\underline{n} = 27$)	8.2 \pm 0.7	9.0 \pm 0.7	8.6 \pm 0.4	9.5 \pm 0.5
Fainters ($\underline{n} = 3$)	9.1 \pm 0.4	9.9 \pm 0.6	8.7 \pm 0.3	9.9 \pm 0.5
NE (pg•ml ⁻¹)				
Nonfainters ($\underline{n} = 26$)	498 \pm 178	747 \pm 297	368 \pm 136	683 \pm 212
Fainters ($\underline{n} = 3$)	658 \pm 327	858 \pm 520	469 \pm 187	918 \pm 417

Table 4-30--continued.

	Pre-training		Post-training	
	Rest	Tilt	Rest	Tilt
EPI (pg•ml ⁻¹)				
Nonfainters (<u>n</u> = 26)	24.3 ± 50.6	14.1 ± 31.2	7.0 ± 17.5	21.2 ± 35.5
Fainters (<u>n</u> = 3)	28.0 ± 48.5	140.3 ± 27.0	17.3 ± 30.0	21.0 ± 36.4

Values are mean ± S.D.

PV = Plasma Volume; BV = Blood volume; RCV = Red cell volume; ACTH = Adrenocorticotrophic hormone; ALDO = Aldosterone; AVP = Vasopressin, K⁺ = Potassium; Na⁺ = Sodium; PROT = Protein; NE = Norepinephrine; EPI = Epinephrine.

concentrations declined substantially. Similarly, fainters had larger increases in ACTH than nonfainters during tilt at T1 ($p < 0.01$) and T3 ($p < 0.01$). At T1, the correlations between the percentage change in HR during tilt and the percentage change in ACTH and AVP were -0.88 ($p = 0.31$) and -0.93 ($p = 0.23$), respectively. Similarly, the correlations between the percentage change in SBP during tilt and the percentage change in ACTH and AVP were -1.0 ($p = 0.06$) and -1.0 ($p = 0.02$), respectively.

Another difference between the fainters and the nonfainters was in the EPI response to tilt. Fainters increased EPI during tilt at T1 by 401% ($p = 0.09$) while the change in EPI secretion in the nonfainters could be ascribed to random variation ($p = 0.36$). The EPI response of fainters during tilt was decreased at T3 ($p = 0.06$).

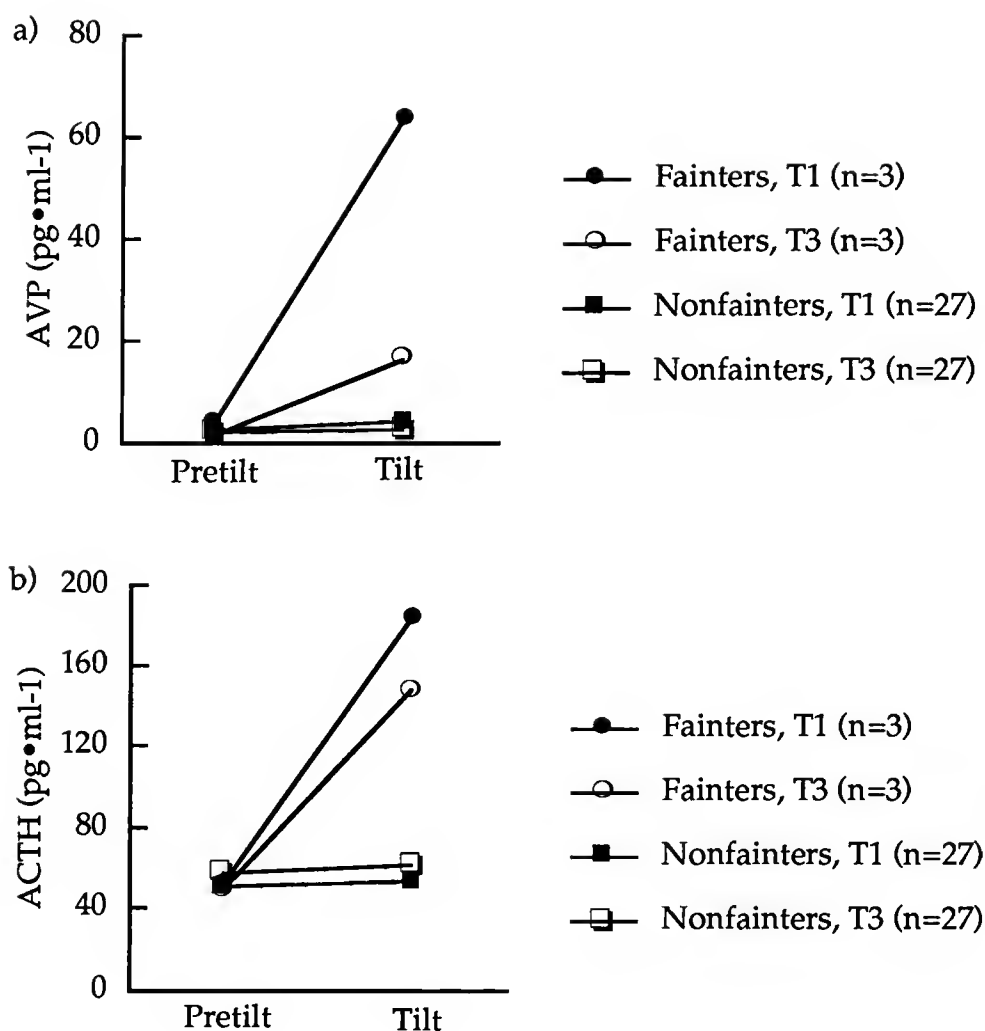


Figure 4-10. Hormonal responses of fainters and nonfainters to supine rest (pretilt) and 70° head-up tilt before (T1) and after (T3) 6 months of exercise training: a) vasopressin (AVP); b) adrenocorticotrophic hormone (ACTH).

Responses to the Cough Test

Analyses to Average Data

The overall responses to the cough test (averaged over tests and groups) were calculated and are shown in Table 4-31. In order to determine whether the values from the three cough trials conducted during both supine rest and during tilt could be combined to yield representative values for

supine and tilt, a repeated measures ANOVA was performed. The probability of a *type I* error in detecting a time effect among the three cough trials during both rest and tilt is listed in Table 4-32. Where the *type I* error probabilities were high, it was concluded that any differences among the three trials were due to random variation.

Table 4-31. Overall Responses to Three Supine and Three Tilt Cough Trials, Values Averaged Over Tests and Groups ($\underline{n} = 24$).

	Rest R-R (sec)	Min. R-R (sec)	Δ R-R (Rest - Min.) (sec)	Time to Min. R-R (sec)	Interval of Min. R-R
Supine					
1	0.96 ± 0.14	0.78 ± 0.11	0.18 ± 0.08	3.33 ± 1.53	4.15 ± 1.73
2	0.95 ± 0.13	0.79 ± 0.11	0.15 ± 0.05	3.43 ± 1.82	4.11 ± 2.14
3	0.96 ± 0.14	0.81 ± 0.11	0.15 ± 0.07	3.13 ± 1.54	3.79 ± 1.93
Mean	0.96 ± 0.14	0.79 ± 0.11	0.16 ± 0.07	3.13 ± 1.26	3.83 ± 1.46
Tilt					
1	0.83 ± 0.15	0.70 ± 0.12	0.13 ± 0.06	4.64 ± 2.27	6.40 ± 3.07
2	0.81 ± 0.14	0.70 ± 0.14	0.10 ± 0.05	5.11 ± 7.02	5.15 ± 1.96
3	0.81 ± 0.15	0.70 ± 0.12	0.11 ± 0.06	4.03 ± 2.30	5.79 ± 3.40
Mean	0.82 ± 0.14	0.70 ± 0.12	0.11 ± 0.05	4.15 ± 1.61	5.80 ± 2.24

Values are mean \pm S.D.

Several of the tests, however, produced low *type I* error rates. An inspection of the raw data showed that the detected differences were usually small and physiologically not important. For example, the difference among the three supine resting R-R intervals was 0.01 seconds. The difference in the HRs calculated from these intervals was $0.7 \text{ b} \cdot \text{min}^{-1}$. The difference between the highest and lowest resting R-R during tilt was 0.02 seconds, resulting in a HR difference of $1.8 \text{ b} \cdot \text{min}^{-1}$. The minimum R-R interval values during

Table 4-32. Analyses to Average Cough Data: *Type I* Error Rates for Detecting a Difference Among the Three Cough Trials for Supine and Tilt Cough Tests ($n = 24$).

	Rest R-R	Min. R-R	Δ R-R (Rest - Min.)	Time to Min. R-R	Interval of Min. R-R
Supine	0.08	<0.01	0.41	0.45	<0.01
Tilt	<0.01	0.53	0.05	0.41	<0.01

supine rest ranged from 0.78 to 0.81 seconds, which resulted in a HR difference of $2.8 \text{ b} \cdot \text{min}^{-1}$. The Δ R-R during tilt ranged from 0.10 to 0.13 seconds. When the HRs for the respective resting and minimum R-R values were calculated and the HR difference calculated, the values varied from 11.6 to $13.4 \text{ b} \cdot \text{min}^{-1}$ (range = $1.8 \text{ b} \cdot \text{min}^{-1}$).

Both supine and tilt cough trials resulted in a low probability of a *type I* error in detecting a time effect for the variable “interval of minimum R-R”. This represents the interval after the cessation of coughing during which the minimum R-R interval occurred. Due to the method of measuring this variable, the accuracy of measurement was at best within ± 1 interval. The difference between the largest and smallest intervals for the supine trials was 0.36 intervals, while the difference for the tilt trials was 1.25 intervals. This latter value would calculate to a difference of approximately 1 second. Therefore, because of the relatively minor differences among trials for the five major cough test variables, the values for the supine and tilt trials were each averaged to yield a single representative value. These values are shown in Table 4-33.

Table 4-33. Mean Supine and Tilt Cough Variable Values for Control, Treadmill, and Treadmill/Resistance Training Groups Averaged Over Three Supine and Three 70° Head-up Tilt Cough Trials Before (T1) and After (T3) 6 Months of Training ($n = 24$).

	Rest R-R (sec)	Min. R-R (sec)	Δ R-R (Rest-Min) (sec)	Time to Min. R-R (sec)	Interval of Min. R-R
Control ($n = 6$)					
T1 Supine	0.98±0.11	0.81±0.13	0.18±0.06	3.27±0.67	4.1±0.6
T3 Supine	1.00±0.09	0.83±0.10	0.16±0.08	3.76±1.49	4.3±1.5
T1 Tilt	0.84±0.11	0.71±0.12	0.13±0.04	3.61±1.13	5.3±2.5
T3 Tilt	0.83±0.11	0.72±0.08	0.11±0.05	4.16±2.48	5.6±3.2
Treadmill ($n = 9$)					
T1 Supine	0.84±0.12	0.71±0.09	0.14±0.05	2.52±1.44	3.5±1.9
T3 Supine	0.92±0.10	0.77±0.09	0.15±0.06	2.95±1.71	3.8±2.4
T1 Tilt	0.74±0.10	0.64±0.08	0.10±0.04	3.17±1.38	4.9±2.1
T3 Tilt	0.79±0.11	0.69±0.08	0.10±0.05	4.16±1.96	6.0±2.9
Treadmill/Resistance ($n = 9$)					
T1 Supine	1.00±0.18	0.82±0.16	0.18±0.10	2.57±0.82	3.1±1.0
T3 Supine	1.02±0.18	0.83±0.13	0.19±0.10	3.99±2.33	4.5±2.5
T1 Tilt	0.84±0.20	0.71±0.17	0.13±0.08	4.06±1.73	5.5±2.2
T3 Tilt	0.87±0.21	0.76±0.18	0.11±0.06	5.68±3.40	7.5±4.6

Values are mean \pm S.D.

Analyses of Cough Responses

The results of the ANOVA performed to assess group differences in initial values indicated a large *type I* error rate for the supine values of minimum R-R ($p = 0.32$), Δ R-R ($p = 0.13$), time to minimum R-R ($p = 0.25$), and interval of minimum R-R ($p = 0.27$). Large *type I* error rates were also generated for the tilt values of resting R-R ($p = 0.29$), minimum R-R ($p = 0.41$), Δ R-R ($p = 0.48$), time to minimum R-R ($p = 0.45$), and interval of minimum R-R ($p = 0.83$). Thus, any differences in these two variables at the start of the

training program were due to random variation. However, the probability of a *type I* error for the supine resting R-R analysis was small ($p = 0.04$). Post hoc analysis using Duncan's multiple range test indicated that TREAD/RESIST had a higher mean resting R-R (lower HR) than TREAD at the start of the program. When gender was used as a covariate in the T1 analysis, the resulting high p -value ($p = 0.30$) indicated that once gender was accounted for any difference among groups was due to random variation.

The effect of training on all cough variables was therefore analyzed with an ANCOVA design using the T1 measure as the covariate. The ANCOVA results indicated that the changes with training for all cough variables could be ascribed to random variation. *Type I* error rates generated in the analyses for supine variables are as follows: resting R-R, $p = 0.26$; minimum R-R, $p = 0.71$; Δ R-R, $p = 0.76$; time to minimum R-R, $p = 0.64$; and interval of minimum R-R, $p = 0.79$. *Type I* error rates generated in the analyses for tilt variables are as follows: resting R-R, $p = 0.42$; minimum R-R, $p = 0.66$; Δ R-R, $p = 0.52$; time to minimum R-R, $p = 0.55$; and interval of minimum R-R, $p = 0.62$.

Inspection of the raw data (Table 4-33) shows that TREAD increased supine resting R-R by 0.09 seconds (10.5%). This calculates to a $6.6 \text{ b} \cdot \text{min}^{-1}$ decrease in the supine resting HR, from 69.8 to 63.2 $\text{b} \cdot \text{min}^{-1}$. Increases in supine resting R-R for TREAD/RESIST and CONT were 3.0% and 1.0%, respectively. Increases exhibited by TREAD, TREAD/RESIST, and CONT in the minimum supine R-R were 8.1% (0.06 seconds, $6.1 \text{ b} \cdot \text{min}^{-1}$ decrease), 1.2% (0.01 seconds, $0.9 \text{ b} \cdot \text{min}^{-1}$ decrease) and 1.2% (0.01 seconds, $0.9 \text{ b} \cdot \text{min}^{-1}$ decrease), respectively.

Increases in resting and minimum R-R during tilt for TREAD were 0.05 seconds (6.8%, $5.2 \text{ b} \cdot \text{min}^{-1}$ decrease) and 0.04 (6.3%, $5.6 \text{ b} \cdot \text{min}^{-1}$ decrease)

seconds, respectively. There was a small increase in resting R-R during tilt for TREAD/RESIST (0.03 seconds, 3.6%, $1.4 \text{ b} \cdot \text{min}^{-1}$ decrease) but a somewhat larger increase for the minimum R-R (0.05 seconds, 7.0%, $5.6 \text{ b} \cdot \text{min}^{-1}$ decrease). The control group had small increases in both resting and minimum R-R during tilt: 0.02 seconds (2.5%, $1.8 \text{ b} \cdot \text{min}^{-1}$ decrease) and 0.1 seconds (1.4%, $1.2 \text{ b} \cdot \text{min}^{-1}$ decrease), respectively.

Because training did not affect resting R-R, minimum R-R, Δ R-R, time to minimum R-R, and interval of minimum R-R, analysis of the effect of tilt on these variables was performed in a repeated measures analysis using mean values averaged over tests and groups. Results indicated that tilt resulted in a decrease in resting R-R ($p < 0.01$), minimum R-R ($p < 0.01$), and Δ R-R ($p < 0.01$), while time to minimum R-R ($p < 0.01$) and interval of minimum R-R ($p < 0.01$) increased. It must be noted, however, that the decrease in the Δ R-R with tilt is due entirely to the decrease in the resting R-R, since a given Δ R-R at a lower baseline translates to a greater change in HR. The average change in supine HR from resting to minimum was $13.4 \text{ b} \cdot \text{min}^{-1}$ while the average change in tilt HR from resting to minimum was $12.5 \text{ b} \cdot \text{min}^{-1}$. In addition, the higher interval of minimum R-R during tilt is due partially to the faster HR. A summary of the effect of tilt and exercise training on the responses to the cough test is presented in Table 4-34.

Table 4-34. Summary of the Effect of Tilt and Training on the Responses to the Cough Test.

Variable	Response to Tilt	Response to Training
Resting R-R	↓	→
Minimum R-R	↓	→
Δ R-R	↓	→
Time to Minimum R-R	↑	→
Interval of Minimum R-R	↑	→

↓ = $p \leq 0.05$, decrease in response as a result of tilt

↑ = $p \leq 0.05$, increase in response as a result of tilt

→ = $p \leq 0.05$, no change in response after 6 months of exercise training

Analyses of Beat by Beat Data

R-R intervals were recorded for one minute after the cessation of cough; a maximum of 40 post-cough beats were measured. R-R interval measurements were converted to HR measurements using the formula $HR = 60/R-R$. Due to the large number of variables (40 beats/position, 2 positions/test [supine, tilt], and 2 tests [T1,T3]), multivariate analyses could not be performed. Therefore, every group of five beats was averaged to provide a representative value; these values are shown in Table 4-35.

A repeated measures analysis comparing each of these averaged values to the resting value was performed for each group and test. This analysis was designed to indicate the recovery to resting heart rate levels after coughing. The results are indicated in Table 4-35 and illustrated in Figures 4-11 through 4-13. The inconsistent results from CONT are most likely due to the

Table 4-35. Heart Rate Values Averaged Every Five Beats for 40 Beats Post-Cough for Control, Treadmill, and Treadmill/Resistance Groups for Supine and 70° Head-up Tilt Cough Tests Before (T1) and After (T3) 6 Months of Training ($n = 24$).

Group/Beats	T1		T3	
	Supine	Tilt	Supine	Tilt
Control ($n = 6$)				
Rest	61.2± 6.2	71.4± 8.2	60.1±5.0	72.3±8.5
1-5	74.1±13.2*	84.0±14.3*	70.1±8.0*	80.9±9.4*
6-10	71.3±13.9*	84.0±17.7*	66.9±6.7*	81.3±9.1*
11-15	65.8±13.5	80.7±17.7*	64.2±6.1*	78.2±8.2*
16-20	63.1± 9.2	77.0±15.6	62.8±7.2*	74.8±8.1*
21-25	62.0± 7.5	75.2±14.1	62.0±7.5	74.1±9.3
26-30	61.6± 7.8	74.9±13.4	61.8±6.4	74.3±8.8
31-35	62.6± 7.4	74.5±11.3	61.0±6.1	74.4±8.3
36-40	61.9± 7.1	73.6±10.5	60.7±6.5	74.5±7.0
Treadmill ($n = 9$)				
Rest	71.4± 8.9	81.1± 9.7	65.2±6.4	75.9± 9.2
1-5	83.8±13.0*	92.7±14.4*	76.0±8.1*	85.3±10.9*
6-10	80.4±14.8*	92.6±14.6*	72.5±9.8*	86.0±12.2*
11-15	74.5±14.7*	89.1±16.2*	68.1±8.4*	83.7±12.3*
16-20	73.0±14.4	85.9±16.7*	65.2±7.5	79.7±12.6*
21-25	72.3±14.4	84.6±17.4	66.2±7.8	78.0±12.1
26-30	72.2±13.8	84.0±17.3	65.9±7.8	78.6±11.9
31-35	71.6±13.5	84.8±16.3	66.1±7.4	78.6±11.8
36-40	71.6±12.2	84.4±15.3	66.1±7.0	78.9±11.8
Treadmill/Resistance ($n = 9$)				
Rest	60.2± 9.2	71.4±13.7	58.8± 8.8	69.0±13.4
1-5	73.3±12.9*	83.8±16.5*	71.0±10.8*	78.6±15.8*
6-10	70.9±12.6*	85.4±16.2*	69.6±10.7*	79.2±15.5*
11-15	67.3±11.6*	82.4±15.9*	64.3±11.2*	76.8±16.3*
16-20	65.2±10.9*	78.1±16.0*	61.9±10.6*	73.6±17.6
21-25	64.0±10.2*	76.4±15.5	61.2±11.1	73.4±15.7
26-30	62.2± 9.5	76.6±14.5	60.9±10.8	72.9±14.7
31-35	62.4± 9.8	76.5±14.5	60.8±11.5	73.8±14.7
36-40	61.2±10.1	76.1±15.1	60.5±12.1	73.5±15.2

Values are mean ± S.D.

* $p \leq 0.05$, greater than rest

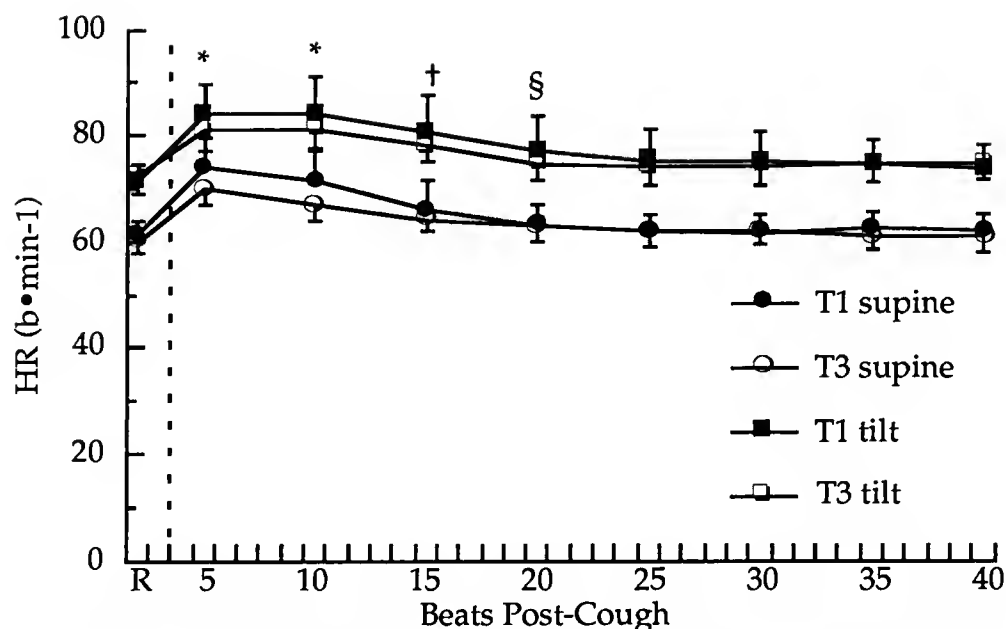


Figure 4-11. Heart rate (HR) response to cough test in supine and 70° head-up tilt positions by control group before (T1) and after (T3) 6 month training protocol. Data points represent the average HR calculated every 5 beats after cessation of coughing. (R = Rest, $n = 6$)

* $p \leq 0.05$, greater than rest in all tests

† $p \leq 0.05$, greater than rest for T3 supine, T1 tilt, and T3 tilt tests

§ $p \leq 0.05$, greater than rest for T3 supine and T3 tilt tests

variability at T1. However, the results for TREAD are similar for T1 and T3 and show that recovery to resting HR was achieved by beat 16-20 in the supine position and by beat 21-25 in the 70° head-up tilt position.

The results for TREAD/RESIST are somewhat different in that they show a faster recovery in the 70° head-up position at both T1 and T3. In addition, recovery is faster by approximately five beats in both the supine and tilt positions at T3.

A 4 X 3 (test X group) repeated measures analysis was performed at each time point; the four tests were T1 supine, T1 tilt, T3 supine, and T3 tilt. Results are presented in Table 4-36. The high error rates for a *test X group* interaction at all points indicates that the relationship among the HR values for supine and tilt cough tests at T1 and T3 was similar for all groups. The low

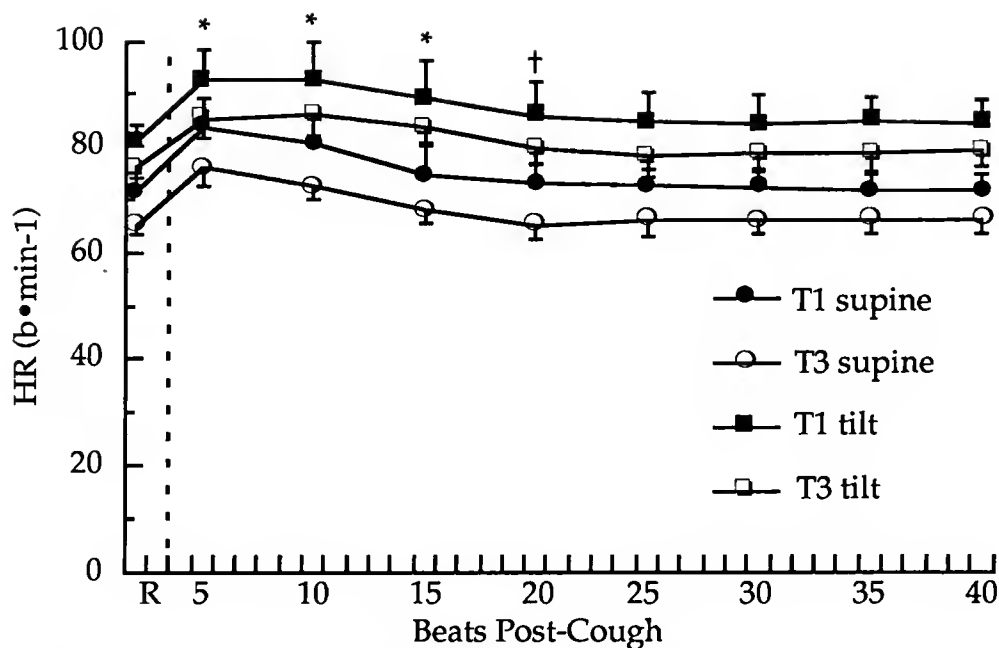


Figure 4-12. Heart rate (HR) response to cough test in supine and 70° head-up tilt positions by treadmill exercise group before (T1) and after (T3) 6 month training protocol. Data points represent the average HR calculated every 5 beats after cessation of coughing. (R = Rest, $\underline{n} = 9$)

* $p \leq 0.05$, greater than rest in all tests

† $p \leq 0.05$, greater than rest in T1 tilt and T3 tilt tests

type I error rates at all points in the “Supine T1 to Tilt T1” and “Supine T3 to Tilt T3” columns indicates that the HR at each point during the tilt cough test was greater than the HR during the respective supine cough test (Table 4-37). In the comparison of the supine T1 and supine T3 tests and of the tilt T1 and tilt T3 tests, the low *type I* error rates through beats 16-20 indicate that the initial response to cough was greater at T1 than T3 (Table 4-37) for both the supine and tilt cough tests. With the exception of the supine HR value at beats 31-35, the HR responses between the two tests (T1 and T3) were similar for both the supine and cough tests after beat 20.

Table 4-36. Probabilities for *Type I* Error for Detecting a Difference in Heart Rate Values at Each Time Point Post-Cough During Supine and 70° Head-up Tilt Cough Tests Before (T1) and After (T3) 6 months of Exercise Training ($\underline{n} = 24$).

	Test X Group*	Time*	Supine T1 to Tilt T1†	Supine T3 to Tilt T3†	Supine T1 to Supine T3†	Tilt T1 to Tilt T3†
Rest	0.48	<0.01	<0.01	<0.01	0.02	0.07
Beat 0-5	0.55	<0.01	<0.01	<0.01	<0.01	<0.01
6-10	0.46	<0.01	<0.01	<0.01	0.02	0.01
11-15	0.90	<0.01	<0.01	<0.01	0.07	0.04
16-20	0.70	<0.01	<0.01	<0.01	0.05	0.06
21-25	0.87	<0.01	<0.01	<0.01	0.11	0.12
26-30	0.77	<0.01	<0.01	<0.01	0.11	0.11
31-35	0.93	<0.01	<0.01	<0.01	0.05	0.10
36-40	0.66	<0.01	<0.01	<0.01	0.15	0.24

* Wilks' Lambda

† Single-degree-of-freedom contrast, analysis of mean difference

Table 4-37. Heart Rate Response to Supine and 70° Head-up Tilt Cough Tests Before (T1) and After (T3) 6 Months of Exercise Training, Values Averaged Over Groups for Every Five Beats for 40 Beats Post-Cough ($\underline{n} = 24$).

	Supine T1	Tilt T1	Supine T3	Tilt T3
Rest	66.0±11.4	77.1±13.4	62.5±8.2	74.2±11.6
Beat 0-5	77.5±13.4	87.2±15.2	72.7±9.2	81.8±12.3
6-10	74.6±14.0	87.8±15.8	70.0±9.4	82.4±12.6
11-15	69.6±13.3	84.5±16.2	65.7±9.0	79.8±12.8
16-20	67.6±12.3	80.7±16.0	63.4±8.5	76.3±13.4
21-25	66.6±11.9	79.2±15.8	63.3±9.0	75.4±12.5
26-30	65.8±11.7	79.0±15.3	63.0±8.7	75.5±12.0
31-35	65.9±11.4	79.1±14.7	62.8±8.9	75.8±11.8
36-40	65.3±11.1	78.6±14.4	62.7±9.3	75.9±11.9

Values are mean ± S.D.

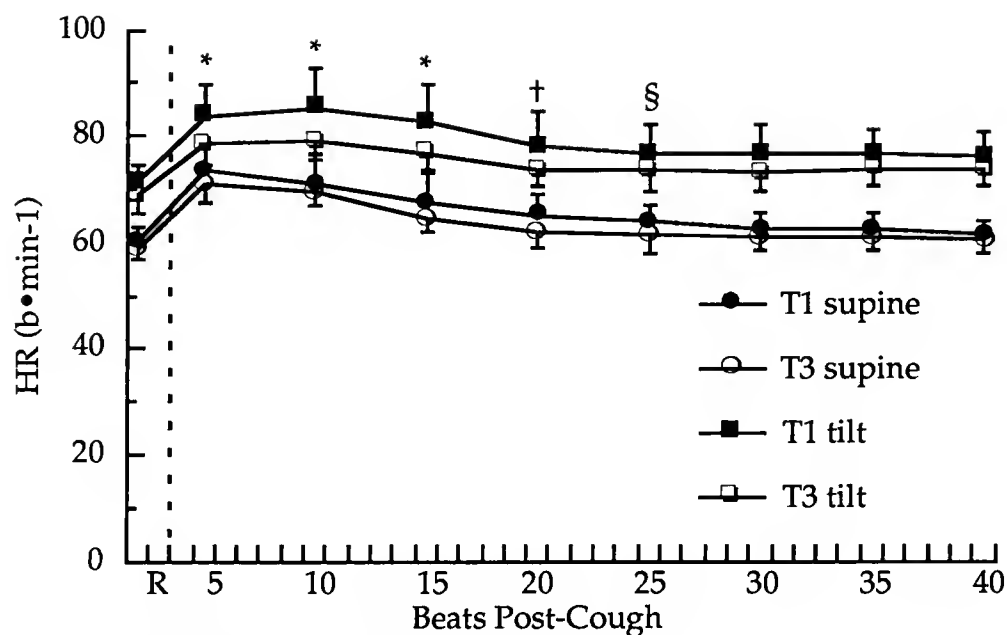


Figure 4-13. Heart rate (HR) response to cough test in supine and 70° head-up tilt positions by treadmill/resistance exercise group before (T1) and after (T3) 6 month training protocol. Data points represent the average HR calculated every 5 beats after cessation of coughing. (R = Rest, $\underline{n} = 9$)

* $p \leq 0.05$, greater than rest in all tests

† $p \leq 0.05$, greater than rest in T1 tilt and T3 supine tests

§ $p \leq 0.05$, greater than rest in T1 supine test

CHAPTER 5 DISCUSSION AND CONCLUSIONS

Introduction

This investigation was the first longitudinal study to investigate the effect of exercise training on the cardiovascular and hormonal responses to orthostasis in the elderly. Cross-sectional and longitudinal studies in younger individuals have suggested that either weight training (Shvartz, 1968a, 1969; Smith et al., 1988; Smith & Raven, 1986) or endurance training with a resistive component (Convertino et al., 1984; Greenleaf et al., 1985; Shvartz et al., 1981) could provide better maintenance of blood pressure during an orthostatic challenge. The present study used a) uphill treadmill walking and b) uphill treadmill walking in conjunction with selected resistance exercises, to determine if one of these types of programs could positively affect orthostatic responses in men and women over 60 years of age. Proposed mechanisms for training-induced adaptations included increased plasma volume, increased muscle mass, increased baroreceptor responsiveness, and altered neuroendocrine responses.

Maximal aerobic power was increased by 16.4% and 13.7% in the treadmill (TREAD) and the treadmill plus resistance (TREAD/RESIST) groups, respectively. TREAD/RESIST increased strength in biceps curl and triceps extension by 26% and 30%, respectively. This is in agreement with data showing that improvements in aerobic power and strength average 15-30% and 25-30%, respectively, in younger individuals (ACSM, 1990; Fleck &

Kramer, 1987) and indicates that older individuals can make comparable relative gains in health and fitness parameters with appropriately designed programs.

Exercise Training and Cardiovascular Responses to Head-up Tilt

Heart Rate, Stroke Volume, and Cardiac Output

Changing from the supine to the upright position translocates approximately 800 ml of blood from the central circulation to the periphery (Blomqvist & Stone, 1983). In response to this venous pooling, central venous pressure, end-diastolic volume and stroke volume (SV) are sequentially reduced; in an attempt to maintain cardiac output (\dot{Q}), heart rate (HR) increases. In the present study, the immediate HR response was a $5.3 \text{ b} \cdot \text{min}^{-1}$ (8.3%) increase; HR then increased progressively to $9.7 \text{ b} \cdot \text{min}^{-1}$ (15.2%) after 15 minutes. These data are consistent with studies finding absolute and relative increases of 10 to $15 \text{ b} \cdot \text{min}^{-1}$, and 10% to 15%, respectively, in older individuals (Jansen et al., 1989; Kenny et al., 1987; Lee et al., 1966; Lye et al., 1990; Shannon et al., 1991; Vargas et al., 1986). This is less than the $10\text{-}30 \text{ b} \cdot \text{min}^{-1}$ (20-25%) increases seen in younger individuals (Beetham & Buskirk, 1958; Convertino et al., 1984; Jansen et al., 1989; Shannon et al., 1991; Vargas et al., 1986). This decreased cardioacceleration capacity is commonly attributed to a reduction in the responsiveness of the high-pressure baroreflex system with age (Frey & Hoffler, 1988; Gribbin et al., 1971) due to arterial rigidity and a reduction in the afferent baroreflex signal, or to a reduction in efferent HR responsiveness (Lipsitz, 1990).

The HR response to tilt was not altered by training: average HR increases at T1 for CONT, TREAD, and TREAD/RESIST were approximately

6, 7, and 8 $\text{b} \cdot \text{min}^{-1}$, respectively, while the increase at T3 was approximately 8 $\text{b} \cdot \text{min}^{-1}$ for all groups. These data are in agreement with those of Shvartz (1968a, 1969), who did not see a difference between control and training groups in the HR response to standing or 90° tilt after 7 weeks of endurance or resistance training. Convertino et al. (1984), on the other hand, found that 8 days of training (2 $\text{h} \cdot \text{d}^{-1}$, 65% $\dot{V}\text{O}_2\text{max}$) decreased the HR response to 60° head-up tilt by 16.7%, from 24 to 20 $\text{b} \cdot \text{min}^{-1}$. The percent change in average tilt HR was negatively correlated ($r = -0.68$) with the percent change in resting PV. In the present study, the same inverse relationship between the percent change in resting PV and the percent change in the HR response to tilt existed ($r = -0.50$; Figure 5-1).

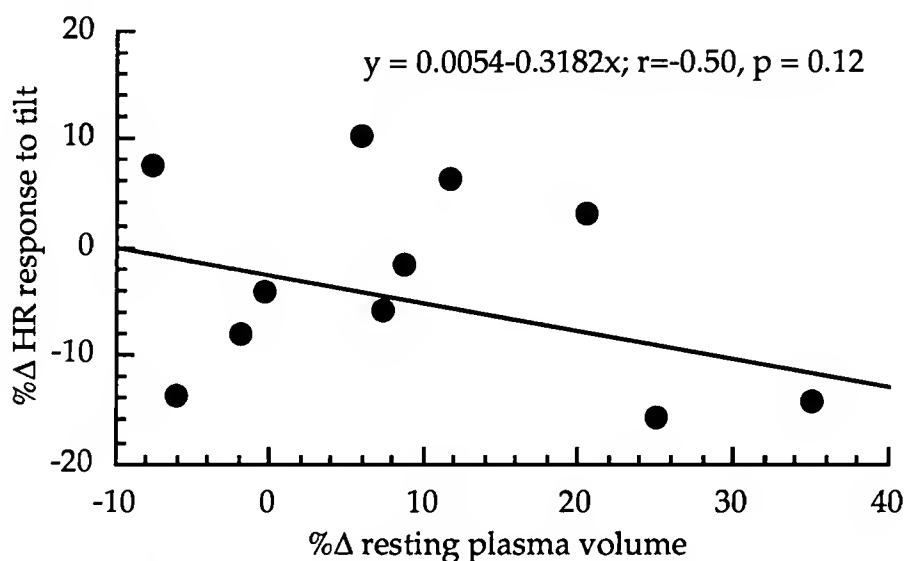


Figure 5-1. Relationship between the relative change in resting plasma volume and the relative change in the HR response to tilt.

In the present study, SV and \dot{Q} were measured by impedance cardiography. While the validity of absolute values measured by impedance has been questioned (Smith, Bush, Wiedmeier, & Tristani, 1970), impedance has been shown to reliably estimate relative changes in SV and \dot{Q} (Ebert,

Eckberg, Vetovec, & Cowley, 1984; Gabriel, Atterhog, Oro, & Ekelund, 1976; Kubicek, Karnegis, Patterson, Witsoe, & Mattson, 1966; Smith et al., 1970). To test the reliability of the impedance technique, correlation coefficients between the T1 and the T3 measurements for resting SV and \dot{Q} for CONT were calculated and were 0.67 (SEE = 8.5 ml, 17.0%) and 0.71 (SEE = 0.44 L•min⁻¹, 14.5%), respectively. The correlations between T1 and T3 for the SV and \dot{Q} measurements made during the remainder of the tilt test (TILT and REC) were 0.70 (SEE = 8.6 ml, 20.6%) and 0.54 (SEE = 0.50 L•min⁻¹, 18.9%), respectively. Thus, in the present study, the impedance technique was moderately reliable in estimating SV and \dot{Q} . An earlier study from our laboratory (Strzepek, 1990) found higher correlations ($r = 0.97$) and lower standard errors (8.7%) between repeated \dot{Q} measurements in a sample of young and old subjects. This may be due to the fact that the repeated measurements in the earlier study were taken within 10 minutes while in the present study, they were taken 6 months apart.

Stroke volume decreases during tilt in the present study (11.9 to 13.6 ml; 23.8% to 27.1%) were consistent with the data from Lee et al. (1966) which showed a 25% decrease in SV in 47 to 82 year old men, but were somewhat less than the 30-40% decreases shown by other investigators (Lye et al., 1990; Shannon et al., 1991; Vargas et al., 1986). The 16-20% decrease in \dot{Q} in the present study was similar to the 11% to 20% decreases documented for older individuals (Lee et al., 1966; Lye et al., 1990; Shannon et al., 1991; Vargas et al., 1986).

Training induced adaptations were found in both the SV and \dot{Q} responses during tilt, with TREAD showing 15.0% and 9.3% increases, respectively, in the mean test responses. At the same time, there was an increase in the magnitude of both the absolute and relative changes from rest

to tilt in both SV and \dot{Q} . TREAD/RESIST, on the other hand, decreased average test \dot{Q} by 9.8%; the magnitude of the both the absolute and relative change from rest to tilt in SV or \dot{Q} was unaltered.

Possible Mechanisms

Increases in SV during tilt may be due to increased preload (i.e., plasma volume [PV]) (Convertino et al., 1984; Shvartz et al., 1981). Due to technical difficulties, however, duplicate PV measurements were made in only four subjects in TREAD. The correlation between the change in tilt SV (measured at the end of tilt) from T1 to T3 and the change in tilt PV was 0.50; the correlation between changes in resting SV and changes in resting PV from T1 to T3 in TREAD was 0.85. Therefore, increased preload was associated with and augmented SV at rest and during an orthostatic challenge in TREAD.

Unexpectedly, TREAD/RESIST had a decrease in the both the resting and average test \dot{Q} at T3. While PV also increased in this group, it appears that other training-induced adaptations occurred which may have masked the expected relation between hypervolemia and increased SV and \dot{Q} . In addition to preload, alterations in cardiac contractility and afterload might explain the decrease in SV and \dot{Q} .

It is not likely that a decrease in contractility is responsible for the decrease in \dot{Q} in TREAD/RESIST. Such a negative inotropic effect would be associated with decreased sympathetic stimulation; although resting NE was decreased in the present study, the reduction was not related to group assignment (Table 4-23). In addition, there is no evidence in the literature to suggest that exercise training results in a decrease in contractility. Previous studies in the elderly (Schocken et al., 1983) have shown that contractile

function, as measured by left ventricular (LV) ejection fraction and LV end-systolic volume, is not changed with training.

A change in afterload is also an unlikely explanation for the decrease in \dot{Q} in TREAD/RESIST since the statistical analyses showed no *test X group* interaction for any of the BP responses (Table 4-12). Therefore, it appears that the decrease in \dot{Q} in TREAD/RESIST is due to factors affecting venous return. With venous return and \dot{Q} compromised, there was an increased reliance on peripheral resistance for the maintenance of BP. However, it is unclear from the present data what mechanism, or combination of mechanisms, is responsible for decreased venous return.

Exercise Training, Resting Plasma Volume and Resting Hormonal Responses

Initial BV, normalized for body weight, was $59.5 \pm 8.6 \text{ ml} \cdot \text{kg}^{-1}$ for CONT, $68.2 \pm 7.6 \text{ ml} \cdot \text{kg}^{-1}$ for TREAD, and $63.6 \pm 8.0 \text{ ml} \cdot \text{kg}^{-1}$ for TREAD/RESIST; this is comparable to the pre-training values of 60-80 $\text{ml} \cdot \text{kg}^{-1}$ found for younger subjects (Convertino et al., 1980a; Convertino et al., 1980b; Convertino et al., 1991; Mack, Thompson, Doerr, Nadel, & Convertino, 1991) and indicates that healthy elderly individuals can maintain a relative BV comparable to younger individuals. While some researchers have shown that resting ALDO levels decrease with age (Crane & Harris, 1976; Gregerman & Bierman, 1981; Saruta et al., 1980) and may play a role in decreasing BV with age, others have shown that resting PRA and ALDO levels are similar for young and old subjects (Vargas et al., 1986). Resting ALDO values in the present sample were similar to values quoted for younger individuals (20-100 $\text{pg} \cdot \text{ml}^{-1}$) (Labhart, 1986) and may be associated with the comparable BV values.

The capacity to increase BV with training also appears to be maintained in the healthy elderly individual. In the present sample, the combined training group (TRAIN) increased both PV and BV by 9.5% (256 ml and 392 ml, respectively) while CONT showed a 1.7% decrease (48 ml) in PV and a 1.5% increase (63 ml) in BV. The relative increases in PV and BV in TRAIN are similar to the 9-12% training-induced increases seen in younger individuals (Convertino et al., 1980a; Convertino et al., 1980b; Convertino et al., 1991). The increase in BV normalized for body weight ($5.7 \text{ ml} \cdot \text{kg}^{-1}$, 8.7%) is similar to training induced increases ($5 \text{ ml} \cdot \text{kg}^{-1}$, 7%) quoted for younger individuals (Convertino, 1991).

Increases in PV in TRAIN were associated with increases in total PROT content ($+20.6 \text{ g}$; $r = 0.99$). If 1 g of protein distributes in 14-15 ml of water (Scatchard, Batchelder, & Brown, 1944), the expected increase in PV would be 288-309 ml, which agrees closely with the measured increase of 256 ml. The changes in PROT content in TRAIN are similar to the 28 g training-induced increase noted by Convertino, Brock, Keil, Bernauer, and Greenleaf (1980), and indicate the importance of plasma proteins in facilitating hypervolemia with training by providing an increased water binding capacity.

Resting levels of AVP, ALDO, and ACTH were not changed with training. This result supports the hypothesis that chronic increases in BV reset the stimulus-response relation between BV (and CVP) and hormonal secretion via cardiopulmonary volume-sensitive receptors. While this relationship has been demonstrated in younger males (27 to 44 years; Convertino et al., 1991), these are the first data from a longitudinal training study to suggest this mechanism in elderly males and females.

Exercise Training and the Hormonal and Plasma Volume Response to Head-up Tilt

In the present study, training did not affect the absolute or relative PV declines during tilt. The PV reductions during tilt at T1 and T3 were 564 ml and 525 ml, respectively, comparable to the pre- and post-training declines of 544 ml and 479 ml seen by Convertino et al. (1984) in an 8-day training regimen in young men. The relative declines were similar at T1 and T3 (20.8% and 18.4%, respectively) but were greater than the 9-13% decreases during tilt reported by Convertino et al. (1984) and Greenleaf et al. (1988). This suggests that elderly individuals undergo a greater challenge during a given orthostatic maneuver than younger individuals.

While the decreases in PV during tilt for TRAIN were nearly identical at T1 and T3, the PV at the end of tilt at T3 was 269 ml greater than the respective T1 measurement because of PV expansion. Thus, an important functional benefit of an increased PV is an expanded reserve to buffer fluid shifts that take place during orthostatic challenges.

Increases in AVP during tilt appear to vary widely (Davies et al., 1976; Huber et al., 1988; Lye et al., 1990; Sander-Jensen et al., 1986; Williams et al., 1988) and may be due to interactions among various stimuli, such as lowered central blood volume (CBV) and pressure, increased sympathetic nervous system activity, and/or hyperosmolality, within each individual. This variability was suggested by Rowe et al. (1982) who postulated the existence of "responders" and "nonresponders" in regard to orthostatic AVP secretion and is reflected in the present data where only 10 of 27 subjects had increases in AVP of greater than $1.0 \text{ pg} \cdot \text{ml}^{-1}$ during tilt. This suggests that atrial receptors are not sole controllers of AVP secretion, but require concomitant hypotension (Mohanty et al., 1985).

A training-induced increase in PV would be expected to attenuate the AVP response to tilt because of better maintenance of CBV and pressure. The peak AVP response to head-up tilt in TRAIN decreased 58% from T1 to T3, while the peak response in CONT increased 24%. This is similar to the results reported by Convertino et al. (1984), where training induced a 38% decline in the AVP response to tilt after training, with a concomitant increase in PV of 12%.

Responses of Fainters

Four subjects were unable to complete the 15 minute tilt duration at T1 due to the onset of presyncopal or syncopal signs and symptoms; all four subjects were able to complete the test at T3. An important consideration when dealing with older individuals who faint or experience presyncopal symptoms during orthostatic maneuvers is whether medications may have contributed to the reaction. While some of the drug regimens of these subjects can cause nausea or fainting (Medical Economics Data, 1992), three of the fainters were under the same medication regimen throughout the study. The fourth subject had the medication dosage (α - blocking agent) increased shortly after the T1 test. This suggests a limited effect of medication on the symptoms experienced at T1. Thus, contributing factors must lie elsewhere.

Stroke Volume and Cardiac Output

Cardiac output appeared to be lower in the fainters, both at rest and consistently throughout the tilt. The lower resting \dot{Q} for the fainters cannot be due to a lower PV since normalized PV measurements for fainters and nonfainters (TRAIN) were $41.9 \text{ ml} \cdot \text{kg}^{-1}$ and $40.6 \text{ ml} \cdot \text{kg}^{-1}$, respectively. A lower \dot{Q} , coupled with a similar BV, suggests an impaired venous return

capacity in the fainters. The mechanism for impaired venous return in the present study is unclear.

Sather et al. (1986) also noted a lower resting \dot{Q} and a smaller \dot{Q} reserve in low tolerant subjects during LBNP. If, as has been hypothesized by Lye et al. (1990), there is a lower minimum limit for SV and \dot{Q} during orthostasis, then the lower resting \dot{Q} in the fainters resulted in a smaller \dot{Q} reserve, which may have contributed to their intolerance.

Plasma volume decreases during tilt at T1 were greater for the fainters (720 ml, 24.6%) than for the nonfainters (526 ml, 19.5%) despite a greater TPR and a shorter duration of tilt. The greater and faster decline in PV may be associated with the onset of presyncopal symptoms since Murray, Krog, Carlson, and Bowers (1967) estimated that presyncopal symptoms could be precipitated by losses of greater than 500 ml from the effective circulation.

At T3, fainters had a 12.5% ($0.32 \text{ L} \cdot \text{min}^{-1}$) increase in resting \dot{Q} and an approximate 15% increase in the lowest \dot{Q} during tilt. Nonfainters increased resting \dot{Q} by only 4.1% ($0.13 \text{ L} \cdot \text{min}^{-1}$) while the \dot{Q} during tilt was nearly identical. The larger increases in \dot{Q} by the fainters cannot be accounted for by PV changes, since both groups increased PV by approximately 9.5%. The augmented \dot{Q} in the fainters may have been related to improved venous return and may have contributed to an increased tilt tolerance by helping to maintain cerebral perfusion and mean arterial pressure.

Blood Pressure

In the present study, there were no obvious differences in the resting blood pressures of the fainters and nonfainters. Tilt initially induced larger increases in SBP, DBP and MAP in the fainters, although the MAP increases (7-8 mmHg) were within the range defined as normal by Frohlich, Tarazi,

Ulrych, Dustan, and Page (1967). Since the \dot{Q} was lower in fainters, this suggests a greater reliance on TPR for MAP regulation.

It has been postulated that orthostatic intolerance in the elderly is inversely related to elevated supine SBP, and may be related more to decreases in SV or to impaired vasoconstriction than to impaired cardioacceleration (Lipsitz, Storch, Minaker, & Rowe, 1985; Smith & Fasler, 1983; Williams, Caird, & Lennox, 1985). The present data do not support the hypothesis that orthostatic intolerance in the elderly is related to impaired vasoconstriction and inversely related to supine SBP. Only male A had a resting SBP > 140 mmHg and a decline in TPR during tilt; this is probably related to α -blockade medication. The other three fainters had supine SBP ranging from 100 to 125 mmHg and increases in TPR during tilt that were proportionally greater than those of the nonfainters.

Hormonal Responses

A higher AVP and ACTH response to tilt or LBNP protocols is a common finding in subjects who become intolerant (Davies et al., 1976; Greenleaf et al., 1988; Harrison et al., 1985; Harrison et al., 1986; Huber et al., 1988; Lee et al., 1966; Norsk et al., 1986; Sander-Jensen et al., 1986). The present data for fainters at T1 are in accord with this finding. Vasopressin secretion is stimulated by hypotension (Share, 1976); thus the heightened response in subjects who experience failure of blood pressure control mechanisms. Fainters in the present study had greater and more rapid absolute and relative decreases in PV during tilt at T1; this may also have augmented the AVP response.

The mechanism for the large increases in AVP and ACTH in the fainters appears to be related to hypotension and the stimulation of

cardiopulmonary receptors. The primary defense against hypotension in the upright position involves the neural control of peripheral resistance. Fainters in the present study had higher resting and orthostatic TPR responses. The higher resting response may be related to a decreased TPR reserve during orthostasis and may prompt failure of this system sooner than experienced in nonfainters. As this defense begins to fail, venous return and left ventricular end-diastolic volume drop, precipitating activation of ventricular stretch receptors. The stimulation of the cardiopulmonary receptors increases AVP secretion and a secondary line of defense is activated whereby there is an attempt to maintain blood pressure and peripheral resistance via hormonal secretion. Adrenocorticotrophic hormone is also stimulated via cardiopulmonary receptors. This relationship between hypotension and increased hormonal secretion is supported by the data which show that correlations between the relative change in HR and the relative changes in ACTH and AVP during tilt for the fainters at T1 were -0.88 and -0.93, respectively, while the relation between the relative change in SBP and the relative changes in ACTH and AVP were -1.0 and -1.0, respectively.

Responses to Cough Test

The HR response to cough is a simple, noninvasive test used to assess the integrity of the reflex arc responsible for cardiac acceleration. Coughing produces increases in intrathoracic pressure ranging between 50 and 250 Torr, and decreases in pulse pressures (Sharpey-Schafer, 1953); the magnitude of the intrathoracic pressure change has been shown to be unrelated to the extent of cardioacceleration (Wei & Harris, 1982). On cessation of cough, there is a decrease in arterial and pulse pressures, and an increase in vasodilation which is associated with increases in right intracardiac pressures. Cardiac

acceleration is thought to be a baroreceptor-mediated response to this hypotension. (Wei & Harris, 1982; Sharpey-Schafer, 1953).

To evaluate the reliability of the cough test, correlation coefficients between the T1 and T3 measurements for CONT were calculated and were as follows: resting R-R, $r = 0.80$ (SEE = 0.08, 8.6%); minimum R-R, $r = 0.69$ (SEE = 0.09, 11.4%); Δ R-R, $r = 0.55$ (SEE = 0.06, 37.5%). Thus, the cough test showed a moderately reliable estimate of resting and minimum R-R measurement in this study. However, the data from TREAD and TREAD/RESIST indicate that there was no change in these parameters in response to cough as a result of training, suggesting that neither endurance nor endurance plus resistance training changes baroreceptor responsiveness in the elderly. This may be due either to age-related decreases in arterial compliance which attenuate afferent baroreceptor signals (Lipsitz, 1990), or to decreases in efferent HR responsiveness to hypotensive stimuli (Gribbin et al., 1971).

Conclusions

Twenty-six weeks of training in 60 to 82 year-old men and women produced significant training adaptations, as evidenced by the 16.4% and 13.7% increases in $\dot{V}O_{2\max}$ in TREAD and TREAD/RESIST, respectively. TREAD had small decreases in body weight and skinfold measurements while TREAD/RESIST increased strength in 1-RM BI and TRI testing, and increased arm circumference.

Endurance training alone produced increases in resting and mean test SV and \dot{Q} in response to 70° head-up tilt. These adaptations may be related to an increased plasma volume and an augmented venous return. Endurance plus resistance training decreased \dot{Q} at rest and in response to 70° head-up tilt and may be related to reduced venous return. Intolerance to tilt at T1 in four

subjects was associated with a lower resting and tilt-induced \dot{Q} , and greater AVP and ACTH secretion. Improved tolerance for the tilt test in these subjects appeared to be related to increases in SV and \dot{Q} at rest and during tilt.

Resting plasma volume was increased by training in the elderly but was not associated with changes in resting hormonal levels. This suggests a change in the stimulus-response relationship between BV and the hormone secretion mediated by volume-sensitive receptors. The hormonal response to tilt was unchanged by training except for a decrease in the AVP response at T3; this may be related to increases in central blood volume.

Directions for Future Research

While the finding of an increase in SV and \dot{Q} in TREAD was not surprising, the finding of a reduced \dot{Q} in TREAD/RESIST was unexpected. Therefore, further research on the effect of strength training on cardiac parameters in the elderly is needed. This is particularly true considering the recent inclusion of resistance training in the ACSM's guidelines (1990) for the development and maintenance of fitness in healthy adults. In addition, the recent increase in interest in moderate- to high- intensity resistance training for older adults (Fiatarone et al., 1990; Frontera et al., 1988; Kauffman, 1985) presents an ideal opportunity for study. The effect of resistance training on the cardiac parameters in different subgroups of the elderly (e.g., hypertensive vs. healthy) also deserves study.

The four subjects who experienced pre-syncopal and syncopal symptoms during the tilt test prior to training were all able to complete the tilt test without symptoms after 6 months of training. The improved responses appeared related to increases in SV and \dot{Q} . An important avenue, therefore, for future research is to study the training-induced cardiac,

hormonal, and plasma volume adaptations in a larger group of orthostatically intolerant subjects.

This was the first longitudinal study to investigate the cardiovascular and hormonal responses to orthostasis in the elderly before and after exercise training. It was not possible to investigate all mechanisms potentially affecting the responses. Other areas for future investigation include a) measurement of central venous pressure and forearm vascular resistance to complement measurements of PV and hormonal responses to orthostasis and training, and to determine the influence of training on cardiopulmonary baroreflex control of vascular resistance in the elderly; b) inclusion of both young and elderly individuals in a longitudinal exercise training study to more fully identify the effect of aging on cardiovascular and hormonal adaptations to orthostasis. Investigation of these areas in different subgroups in the elderly (e.g., healthy elderly, hypertensives, elderly with orthostatic hypotension; elderly taking β -blockers) is also important.

APPENDIX A

DEMOGRAPHIC, MEDICAL AND ACTIVITY QUESTIONNAIRES

CENTER FOR EXERCISE SCIENCE
UNIVERSITY OF FLORIDA, GAINESVILLE, FLORIDA 32611
392-9575

DEOMGRAPHIC INFORMATION

NAME _____ DATE ____/____/____
Last First MI Month Day Year

AGE _____ DATE OF BIRTH ____/____/____
Month Day Year

SOCIAL SECURITY # ____-____-____ PHONE _____

HEIGHT _____ in. _____ cm

WEIGHT _____ lb. _____ kg

RESIDENCE _____
Street

City State ZIP Country

REFERRING PHYSICIAN _____

SURGEON (if applicable) _____

HOME PHYSICIAN (if different from referring M.D.) _____

ADDRESS _____
Street

City State ZIP Country

Sex _____ Male
_____ Female

Race _____ White
_____ Black
_____ Asian
_____ Hispanic
_____ Other: _____

Marital Status

☐ Single
☐ Married # years _____
☐ Divorced or separated # years _____
☐ Widowed # years _____

Religion (optional)

☐ Catholic ☐ Hindu
☐ Protestant ☐ Muslim
☐ Jewish ☐ None
☐ Jehovah Witness ☐ Other: _____

Education Completed

☐ 1-8 years ☐ High school graduate
☐ 9-12 years ☐ Bachelor's degree
☐ 13-16 years ☐ Master's degree
☐ 17-18 years ☐ Doctoral degree
☐ more than 18 years

Occupation (list) _____

Present work status

☐ Working full time
☐ Working part time
☐ Not employed - Reason: ☐ Medical ☐ Other
☐ Retired

Indicate your family income before taxes (U.S. dollar equivalent)

☐ less than \$10,000
☐ \$10,000 - \$25,000
☐ \$25,000 - \$50,000
☐ more than \$50,000

STATEMENT OF CONFIDENTIALITY

I understand that information contained on this questionnaire is regarded as confidential, and will not be released without my prior written permission. The information will not be used for the setting of fees. The Center for Exercise Science may, however, use the information for statistical and other research purposes.

Signature

Date

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392-9575

CARDIOVASCULAR HISTORY

NAME _____

ID# _____
DATE _____

Answer the following questions, indicating the month and year of the event or diagnosis where appropriate.

- | | Yes | No | Month/Year |
|--|-------|-------|------------|
| 1. Has a doctor ever told you that you have heart disease? | _____ | _____ | _____/____ |
| 2. Have you ever had a heart attack? | _____ | _____ | _____/____ |
| 3. Have you ever had chest pain? | _____ | _____ | _____/____ |
| 4. Have you ever had cardiac catheterization? | _____ | _____ | _____/____ |
| 5. Have you ever had balloon angioplasty? | _____ | _____ | _____/____ |
| 6. Have you had coronary artery bypass graft surgery? | _____ | _____ | |

If yes, list date and number of grafts:

_____/____ # grafts: ____ 1 ____ 2 ____ 3 ____ 4+
Mo. Yr.

- | | | | |
|--|-------|-------|------------|
| 7. Have you ever had a stroke? | _____ | _____ | _____/____ |
| 8. Do you have hypertension (high blood pressure)? | _____ | _____ | _____/____ |

If yes, how long have you had hypertension?

- _____ less than 1 year
_____ 1-5 years
_____ 6-10 years
_____ more than 10 years

- | | | | |
|-----------------------------------|-------|-------|------------|
| 9. Do you have diabetes mellitus? | _____ | _____ | _____/____ |
|-----------------------------------|-------|-------|------------|

		Yes	No	Month/Year
10.	Do you take insulin for diabetes?	___	___	
	If yes, how long have you taken insulin?			
	___ less than 1 year			
	___ 1-5 years			
	___ 6-10 years			
	___ more than 10 years			
11.	Do you take oral hypoglycemics for diabetes?	___	___	
12.	Do you have a cardiac pacemaker?	___	___	
	If yes, how long have you had a cardiac pacemaker?			
	___ less than 1 year			
	___ 1-5 years			
	___ 6-10 years			
	___ more than 10 years			
13.	Have you had a carotid endarterectomy?	___	___	___/___
14.	Has your doctor ever told you that you have a heart valve problem?	___	___	___/___
15.	Have you had heart valve replacement surgery?	___	___	___/___
	If yes, what heart valves were replaced?	___ mitral	___ aortic	
16.	Have you had cardiomyopathy?	___	___	___/___
17.	Have you had a heart aneurysm?	___	___	___/___
18.	Have you had heart failure?	___	___	___/___
19.	Have you ever suffered cardiac arrest?	___	___	___/___

20. OTHER MEDICAL PROBLEMS: Indicate if you have had any of the following medical problems:

Past	Now	
_____	_____	Alcoholism
_____	_____	Allergies
_____	_____	Anemia
_____	_____	Arthritis
_____	_____	Asthma
_____	_____	Back injury or problem
_____	_____	Blood clots
_____	_____	Bronchitis
_____	_____	Cirrhosis
_____	_____	Claudication
_____	_____	Elbow or shoulder problems
_____	_____	Emotional disorder
_____	_____	Eye problems
_____	_____	Gall bladder disease
_____	_____	Glaucoma
_____	_____	Gout
_____	_____	Headaches
_____	_____	Hemorrhoids
_____	_____	Hernia
_____	_____	Hip, knee, or ankle problems
_____	_____	Intestinal disorders
_____	_____	Kidney disease
_____	_____	Liver disease
_____	_____	Lung disease
_____	_____	Mental illness
_____	_____	Neurologic disorder
_____	_____	OB/GYN problems
_____	_____	Obesity/overweight
_____	_____	Phlebitis
_____	_____	Prostate trouble
_____	_____	Rheumatic fever
_____	_____	Seizure disorder
_____	_____	Stomach disease
_____	_____	Thyroid disease
_____	_____	Tumors or cancer - List type: _____
_____	_____	Ulcers
_____	_____	Other - specify: _____

21. Surgical Procedures: Indicate if you had had any of the following surgeries, and if so, the appropriate date.

	Yes	No	Month/Year
Adhesion repair	_____	_____	_____/____
Appendectomy	_____	_____	_____/____

21. Surgical Procedures (continued)

	Yes	No	Month/Year
Back surgery	_____	_____	____/____
Bladder surgery	_____	_____	____/____
Bowel surgery	_____	_____	____/____
Breast surgery	_____	_____	____/____
Cataract surgery	_____	_____	____/____
Gall bladder surgery	_____	_____	____/____
Hemorrhoid surgery	_____	_____	____/____
Joint surgery	_____	_____	____/____
Kidney surgery	_____	_____	____/____
Lung surgery	_____	_____	____/____
OB/GYN surgery	_____	_____	____/____
Prostate surgery	_____	_____	____/____
Stomach surgery	_____	_____	____/____
Other - specify: _____	_____	_____	____/____

22. Medications: Indicate the medicines you currently use on a regular basis.

	Yes	No
Allergy medicines/antihistamines	_____	_____
Antacids	_____	_____
Antibiotics	_____	_____
Anti-arrhythmics	_____	_____
Anti-inflammatory agents	_____	_____
Aspirin	_____	_____
Asthma medicines	_____	_____
Beta blockers	_____	_____
Birth control pills (# years: _____)	_____	_____
Blood pressure medicines	_____	_____
Blood thinners	_____	_____
Cortisone	_____	_____
Diabetes medicines/insulin	_____	_____
Diuretics/"water pills"	_____	_____
Gout medicines	_____	_____
Heart medicines	_____	_____
Hormones/estrogen	_____	_____
Laxatives	_____	_____
Nitroglycerin	_____	_____
Pain medicines	_____	_____
Psychiatric medicines/anti-depressants	_____	_____
Sedatives/sleeping pills	_____	_____
Seizure medicines	_____	_____
Thyroid medicines	_____	_____
Tranquilizers	_____	_____
Vitamins/iron	_____	_____
Other - specify: _____	_____	_____

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FAMILY HEALTH HISTORY

NAME _____

ID# _____

DATE _____

- A. If any members of your immediate family have or have had any of the following conditions, indicate their age at the time of the event:

	Father	Mother	Brother(s)	Sister(s)
Heart Attack	_____yr	_____yr	_____yr	_____yr
Stroke	_____yr	_____yr	_____yr	_____yr
Coronary Artery Disease	_____yr	_____yr	_____yr	_____yr
If deceased, not age at time of death	_____yr	_____yr	_____yr	_____yr

- B. Indicate if any members of your immediate family have or have had the following conditions by marking the appropriate lines:

	Father	Mother	Brother(s)	Sister(s)
High Blood Pressure	_____yr	_____yr	_____yr	_____yr
High Cholesterol	_____yr	_____yr	_____yr	_____yr
Diabetes	_____yr	_____yr	_____yr	_____yr
Obesity	_____yr	_____yr	_____yr	_____yr

NAME _____

1. Please indicate your usual activities.

[illegible]

2. Does your usual job require sustained physical activity?

____ Yes ____ No ____ Not employed ____ Not applicable (retired)

3. How would you rate your physical fitness (endurance)?

low			medium			high
1	2	3	4	5	6	7

4. How would you rate your strength?

low			medium			high
1	2	3	4	5	6	7

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TOBACCO HISTORY

NAME _____

ID# _____
DATE _____

1. Have you ever used any tobacco product on a regular basis?

_____ Yes
_____ No

IF YES: Continue

IF NO: Stop here

2. What form(s) of tobacco do/did you regularly use?

Past	Now		# years	Amount/Day
_____	_____	Cigarettes	_____	_____ packs
_____	_____	Cigars	_____	_____ cigars
_____	_____	Pipe	_____	_____ pipefuls
_____	_____	Chewing tobacco	_____	_____ chaws
_____	_____	Snuff	_____	_____ dips

3. Are you a former smoker?

_____ Yes
_____ No

IF YES:

- a. How long ago did you stop smoking?

_____ Less than 6 months
_____ 6-12 months
_____ 1-2 years
_____ 3-5 years
_____ 5-10 years
_____ more than 10 years

- b. What was your reason for stopping?

_____ Doctor's advice
_____ Concern about health
_____ Heart surgery or cardiac event
_____ Family pressure
_____ Education program
_____ Other - specify: _____

APPENDIX B

INFORMED CONSENT DOCUMENT

CENTER FOR EXERCISE SCIENCE
UNIVERSITY OF FLORIDA, GAINESVILLE, FL 32611
392-9575

Informed Consent to Participate in Research

You are being invited to participate in a research study. This form is designed to provide you with information about this study and answer any of your questions.

1. TITLE OF RESEARCH STUDY

Effects of 6 months of endurance and resistance exercise training on healthy men and women over 60 years of age.

2. PRINCIPAL INVESTIGATOR

Name: Michael L. Pollock, Ph.D.

Telephone Number: 904-392-9575.

3. THE PURPOSE OF THE RESEARCH

The purpose of the study is to determine if you as a healthy person between the ages of 70-89 can adapt to endurance and strength exercise training with improvements in cardiovascular function, strength, orthostatic tolerance (ability of blood pressure reflexes to quickly adapt to changes in posture), and body composition (reduction in body fat, increase in bone density and muscle weight).

4. PROCEDURES FOR THIS RESEARCH

Visit 1: During your first visit to the Center for Exercise Science, the entire study protocol and the time commitment necessary will be explained. An investigator will be available to answer any questions. You will also be given a medical history form and a physical activity questionnaire to take home and complete (30 minutes).

Visit 2: During your second visit, you will undergo an examination by a physician and have your blood pressure and electrocardiogram (ECG) recorded at rest. A 15 ml venous blood sample will be drawn for screening purposes. This is equivalent to approximately 3 teaspoons of blood. There will be a nominal fee of \$45.75 for this blood chemistry screening.

You will then take an exercise test on a treadmill while your ECG and blood pressure are monitored. Every two minutes during this test the exercise will become more difficult, until the physician stops the test because of certain signs or symptoms, or when you are unable to continue

because of fatigue. If you have no cardiovascular or other significant medical abnormalities considered contra-indicative to exercise training, you will be included in the study (2 hours).

Visit 3: Your blood pressure will be measured at rest after 15 minutes of quiet sitting; you will then stand up and your blood pressure will be measured after 1 minute of quiet standing. You will then be familiarized with some of the other equipment and procedures used in some of the later testing sessions. These include a breathing valve used to collect your expired air (Visit 4), a tilt table test (Visit 5), and strength tests (Visit 6). (2 hours).

Visit 4: This visit includes a test of blood pressure reflex sensitivity and a maximal exercise test. The blood pressure reflex sensitivity test consists of a series of intravenous drug infusions which are designed to either slow or speed up the heart rate. The blood pressure response to this change in heart rate will be recorded. To make the drug infusions easier, a needle will be placed in a forearm vein before the test is begun. This needle placement will be done under sterile conditions and kept open with sterile saline for the duration of the test. This needle will also be used for blood sampling during the exercise test.

You will then undergo a second exercise test; it will be similar to the test in Visit 2 except that you will have a rubber mouthpiece in your mouth and a clip on your nose so that your expired air can be collected. This test will be continued until certain signs or symptoms indicate the test should be stopped or you are unable to continue because of fatigue. During this test, measurements of hormones will be made at rest and at maximal exercise. For this it will be necessary to take two small blood samples of approximately 4 teaspoons each (2 hours).

Visit 5: This visit includes measurement of right heart pressure, plasma volume, and a tilt table test. To make all of the tests easier, a needle will be placed in a forearm vein before the first test is begun. This needle placement will be done under sterile conditions and kept open with sterile saline for the duration of the test session. This needle will also be used for plasma volume measurement and for blood sampling during the tilt test.

For the indirect measure of the pressure in your right heart, a pressure gauge will be attached to the needle in your arm. You will simply lie on your right side with your right arm hanging down while the pressure measurement is made.

Measurement of plasma volume will also be made during this session. A special non-toxic dye will be injected into the arm opposite the one with the venous catheter (needle) and a blood sample of approximately 1 1/2 teaspoons will be taken after 10 minutes. You will simply lie on your back on a table during the test.

The tilt test is performed on a special table which can be adjusted to various angles. The tilt test will consist of 30 minutes rest (lying on your back with the tilt table in a level position), 15 minutes of 70° head-up tilt,

and 15 minutes recovery, again lying on your back with the tilt table level. You will have your pulse, blood pressure, cardiac output (amount of blood your heart pumps each minute), stroke volume (amount of blood your heart pumps each beat), and blood flow in the arm and leg made during the entire test. During this test, you will be asked simply to lie quietly and to refrain from conversation except to answer questions from the investigators. A physician will monitor all tests.

In the head-up tilt test, some measurements of blood volume change and hormones will also be made. For this, it will be necessary to take two small blood samples, each less than 1/2 teaspoon, and two small blood samples, each about 4 teaspoons. The total amount of blood taken during the test is about 9 teaspoonfuls (2 1/2 hours).

Visit 6: Your resting blood pressure will again be measured as in Visit 3. Then your body fat and muscle mass will be assessed by measuring skinfold fat thicknesses and circumferences. Body fat and muscle will also be measured with the ultrasound technique which uses sound waves to measure muscle and fat layer thicknesses. The ultrasound technique is non-invasive and consists of putting a sound wave transducer up against the skin at various locations on the body. A 2-dimensional picture of the fat and muscle layers is then printed. Another body composition measurement technique will measure fat and muscle tissue using X-ray methods (DEXA). The DEXA method is non-invasive. You will need only to lie first on your back and then on your side for a total of 20-30 minutes while the scanner arm of the machine records your total and regional bone mineral, fat and lean body mass composition. Muscular strength will be measured by using maximum effort tests for the upper arm, lower back, and legs. Warm-up and gradual increase in workload will be used during strength testing (2 hours).

Visit 7: The distensibility of the veins in your lower leg will be measured. This involves the placement of a thin gauge around your lower leg and the placement of a cuff similar to a blood pressure cuff around your leg just above the knee. Pressure in the cuff will be increased to 30 mmHg, which is much lower than the pressure of cuff inflation during a blood pressure reading (normally about 200 mmHg). The slight change in the size of your lower leg will then be measured. This is a non-invasive test; you will simply need to lie quietly on a table for the test.

You will then walk on the treadmill at 3 submaximal speeds. You will again be using the mouthpiece and nose clip as in Visit 4. At each of the 3 submaximal speeds, you will walk for approximately 6 minutes while your heart rate and expired gases are analyzed. Each 6 minute exercise session will be followed by a 2 minute slow walk (1 1/2 hours).

Visit 8: Resting blood pressure will again be measured. During this visit, the muscle electrical activity in your arm will be recorded with surface electrodes at rest and in response to a light stimulus. The time it takes to respond to a light stimulus will also be recorded.

During this visit, you will also ride a stationary bicycle at several submaximal speeds while the electrical activity in your legs is recorded. Surface electrodes will be placed on your upper right leg. You will pedal the bicycle at each speed for 2 minutes. In between work bouts, you will rest until your heart rate comes down to its resting level (2 hours).

The total amount of blood drawn during all the testing sessions is about 22 teaspoons; this is approximately one-quarter the amount of blood that you would give if you donated a pint of blood.

You will then be randomly assigned to an endurance training group, an endurance and strength training group, or a control group. The control group will not exercise during the study, but will be given the opportunity to train as soon as the study is over.

Endurance exercise training by both exercise groups will be done 3 times per week for 6 months in the Center for Exercise Science on treadmills and/or stair-stepping machines. The exercise intensity will be individually prescribed based on your heart rate response to exercise. The program will start at a very low intensity and short duration and will gradually progress up to 70-80% of your capacity for 40--50 minutes each session. The progression will be based on your response to the program. One of the exercise groups will also do strength training for the arms and lower back. Strength training for the arms will be done 3 times per week in a room adjacent to the Center for Exercise Science on the same days as the endurance exercise training. Strength training for the lower back will be done 1 day each week on one of the endurance exercise training days. Training will begin very slowly and gradually to allow for gradual adaptation. For the arm training, you will perform 8-12 repetitions of 2 exercises on Nautilus™ exercise machines. For the lower back training, you will perform 8-12 repetitions on the MedX™ Lower Back Machine. The progression will be based on your adaptation, with initial intensity being set at a light weight for each machine. The weight lifted will be slowly increased each week until you perceive the training to be moderately hard. Continued increases will be based on your adaptation to training.

Retesting: After 3 months of training, and again at the end of the study, subjects in the exercise and control groups will repeat Visits 4-8.

5. POTENTIAL RISKS OR DISCOMFORTS

Endurance exercise testing and training is associated with a small risk of cardiovascular complications. The risk for exercise testing is about 3-4 non-fatal incidents (events) in 10,000 GXTs and 1 fatal event per 25,000 tests. The Cooper Clinic in Dallas, Texas has had 6 non-fatal and no fatal cardiovascular events in 80,000 exercise tests. Five of 6 events occurred

with persons with known cardiovascular disease. The risks involved with exercise testing for older individuals may be higher than this. The risk will be minimized in this study because all the personnel involved with testing and training are experienced in working with older men and women. In addition, a physician will monitor all of the exercise tests and your blood pressure, heart rate and ECG will be closely monitored during the exercise tests. You can expect some fatigue and breathlessness to accompany the exercise testing at the start, the middle, and end of the study. With regard to exercise training, only 1 fatal event has occurred over the past 15 years of exercise training at the Aerobics Activity Center in Dallas. Their event rate is less than one in over 1,000,000 miles of walking and jogging. Exercise training for older individuals may involve a higher risk. Thus, the risk of serious injury is considered extremely low for both exercise testing and training. In this study, your heart rate and level of exertion will be monitored frequently as you exercise in order to further assure your safety. However, there is the possibility of minor injury, such as pulling a muscle or twisting an ankle or knee, during the exercise training phase of the study.

There is little data on the injury rate in strength training. Our previous experience with strength testing and training in older individuals indicates that the musculoskeletal injury rate is low during strength training. You may, however, experience some minor muscle soreness during training. The injury rate may be higher during strength testing, but the risk in the present study will be kept low by careful warm-up and slow progression. The risk of any cardiovascular complication during strength testing and training is low; studies of participants in recreation sports, which included some weight trainers, showed 1 cardiovascular complication per 495,000 participants.

The risks of drawing blood from a vein include discomfort at the site of needle placement; possible bruising and swelling around the site of needle placement; rarely an infection; and uncommonly, faintness from the procedure. The risk is minimized by the use of sterile techniques and the infusion of sterile saline to keep the catheter open during the duration of their placement. The risk of serious injury with blood drawing and catheterization is therefore quite minimal.

The risks involved in the drug infusions used to test baroreflex sensitivity are minimal. The drugs are used only to change the heart rate within the normal range and the blood pressure response to the change of heart rate will be recorded. A catheter will be in place for this test; aside from the risk of catheter placement, as noted above, there has been no recorded incidence of complications arising from use of this procedure. The safety of the test will be assured by the direct supervision of a physician, and by the availability of drugs to counteract the initial infusions if the need should arise.

During the tilt test, the possibility exists that you may feel nausea, dizziness, lightheadedness, sweating, tunnel vision, or faintness before the

15-minute limit of this test. If this happens, or if your heart rate or blood pressure drop too low, the test will be immediately ended and the table returned to a level position. This should quickly relieve these symptoms. In addition, you will be secured to the tilt table by a wide Velcro band across the hips so there is little danger of falling in the event that you do faint. A physician will monitor all head-up tilt tests.

There is a small X-ray dosage during the DEXA (X-ray) body composition procedure. The dose during a total body scan is less than 0.5 mrem. This exposure is far less than the average radiation exposure of 30 mrem from a chest X-ray and is approximately 0.3% of the average annual per capita exposure in the U.S. This low dosage is due to the low current setting of the apparatus, and the speed of the procedure. In addition, lead oxide shielding surrounds the X-ray tube within the machine and this reduces radiation levels outside the scan area on the body and around the scan table. A quality control test is run every day the machine is used in order to assure that only low levels of radiation are emitted.

6. POTENTIAL BENEFITS TO YOU OR TO OTHERS

You will receive a complete cardiovascular examination and a battery of tests at the start of the study. The results of these studies will be available to your private physician. You will also receive an individualized exercise prescription based on your exercise capacity and the chance to complete a six month training program at no charge and under the close supervision of a highly-qualified research team. Society in general will learn whether endurance and strength exercise can elicit beneficial adaptations with respect to body composition, muscular strength, cardiovascular function, orthostatic tolerance, and blood pressure in healthy men and women over the age of 70.

7. ALTERNATIVE TREATMENT OR PROCEDURES, IF AVAILABLE

You may choose not to participate in the study.

8. GENERAL CONDITIONS

I understand that I will ____/ will not x receive money for my participation in this study. If I am compensated, I will receive _____.

I understand that I will x/ will not ____ be charged additional expenses for my participation in this study. If I am charged additional expenses these will consist of \$45.75 for a blood chemistry and blood lipid screening and for analysis of thyroid hormones.

I understand that I am free to withdraw my/my child's consent and discontinue participation in this research project at any time without this decision affecting my/my child's medical care. If you have any questions regarding your rights as a subject, you may phone 392-3063.

In the event of my/my child sustaining a physical injury which is proximately caused by this experiment, professional medical care received at the J. Hillis Miller Health Center exclusive of hospital expenses will be provided me without charge. This exclusion of hospital expenses does not apply to patients at the Administration Medical Center (VAMC) who sustain physical injury during participation in VAMC-approved studies. It is understood that no form of compensation exists other than those described above.

I also understand that the University of Florida and the Veterans Administration Medical Center will protect the confidentiality of my records to the extent provided by Law. The Study Sponsor, Food and Drug Administration or either Institutional Review Board may ask to review my records; however, the records will remain confidential as only a number and initial will be used.

9. SIGNATURES

I have fully explained to _____ the nature and purpose of the above-described procedure and the benefits and risks that are involved in its performance. I have answered and will answer all questions to the best of my ability. I may be contacted at telephone number 904-392-9575.

Signature of Principal or Co-Principal
Investigator Obtaining Consent

Date

I have been fully informed of the above-described procedure with its possible benefits and risks and I have received a copy of this description. I have given permission for my/my child's participation in this study.

Signature of Patient or Subject of Relative
or Parent or Guardian (specify)

Date

Signature of Child (7 to 17 years of age)

Date

Signature of Witness

Date

APPENDIX C

INSTITUTIONAL REVIEW BOARD APPROVAL LETTER



HEALTH CENTER INSTITUTIONAL REVIEW BOARD
D11-22

UNIVERSITY OF FLORIDA
VICE PRESIDENT FOR HEALTH AFFAIRS

HEALTH SCIENCE CENTER

BOX J-14

Gainesville, Florida • zip 32610-0014

July 19, 1991

TO: Michael L. Pollock, Ph.D., J-277

FROM: B. J. Wilder, M.D., J-14

Chairman, Institutional Review Board

R. Peter Lattate
R. Peter Lattate, Pharm.D.
Vice Chair J-14

SUBJECT: Reapproval of Institutional Review Board
Project # 267-90

Your request to continue your research Project involving human
subjects # 267-90 title: Effects of 6 Months of Endurance Exercise
Training on Healthy Men and Women 70-89
Years of Age

is approved as recommended by the Institutional Review Board. You are reminded that a change in protocol in this project must be approved by resubmission of the project to the Board for approval. Also, the principal investigator must report to the Chair of the Board promptly, and in writing, any unanticipated problems involving risks to subjects or others, such as adverse reactions to biologicals, drugs, radio-isotopes or to medical devices.

If the project has not been completed by 8/24/92 please request renewed approval, which is necessary for continuation of this project.

If it is anticipated that VA patients will be included in this project, or if the project is to be conducted in part on VA premises or performed by any VA employee during VA-compensated time, final approval should be obtained by application to the Veterans Administration Hospital Research Office.

By a copy of this memorandum the chairman of your department is reminded that he is responsible for being informed concerning research projects involving human subjects in his department. He should review the protocols of such investigations as often as he thinks necessary to insure that the experiment is being conducted in compliance with our institution and with DHHS regulations.

CC: B. J. Wilder, M.D.
James E. McGuigan, M.D.
Rhonda Cooper, Pharm.D.
Edward Block, M.D.
Clinical Research Center
DSR

co-PIs: ✓Joan F. Carroll, M.A.
James A. Graves, Ph.D.
David Lowenthal, M.D., Ph.D.
Marian Limacher, M.D.
Scott H. Leggett, M.S.
Victor Convertino, Ph.D.
William Chen, Ph.D.
Myron Miller, M.D.
Charles E. Wood, Ph.D.

J. HILLIS MILLER HEALTH CENTER
College of Medicine • College of Nursing • College of Pharmacy • College of Health Related Professions • College of Dentistry
College of Veterinary Medicine • Veterinary Medical Teaching Hospital • Shands Hospital • Veterans Administration Medical Center

EQUAL EMPLOYMENT OPPORTUNITY/AFFIRMATIVE ACTION EMPLOYER

APPENDIX D

DATA COLLECTION FORMS FOR TILT TEST

CENTER FOR EXERCISE SCIENCE
UNIVERSITY OF FLORIDA, GAINESVILLE, FLORIDA 32611
392-9575

CARDIOVASCULAR DATA, HEAD-UP TILT

Name: _____ Date: _____ T1/T2/T3

Age: _____ Ht.: _____ Wt.: _____ BSA: _____

Hct: Baseline _____ Pre _____ Post _____ Hb: Pre _____ Post _____

HR

SV

Q

CI

HI

Supine					
-15					
-10					
-5					
0					
Tilt					
0					
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					
11					
12					
13					
14					
15					

Recovery

0					
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					
11					
12					
13					
14					
15					

CENTER FOR EXERCISE SCIENCE
UNIVERSITY OF FLORIDA, GAINESVILLE, FLORIDA 32611
392-9575

ARM BLOOD PRESSURE, TILT PROTOCOL

NAME: _____

DATE: _____

TEST: _____

	Systolic	Diastolic
<u>Supine</u>		
-15		
-10		
-5		
0		
<u>Tilt</u>		
0		
1		
2		
3		
4		
5		
10		
15		
<u>Recovery</u>		
0		
1		
2		
3		
4		
5		
10		
15		

COUGH TEST DATA

Pre-cough R-R: _____

Min. R-R: _____

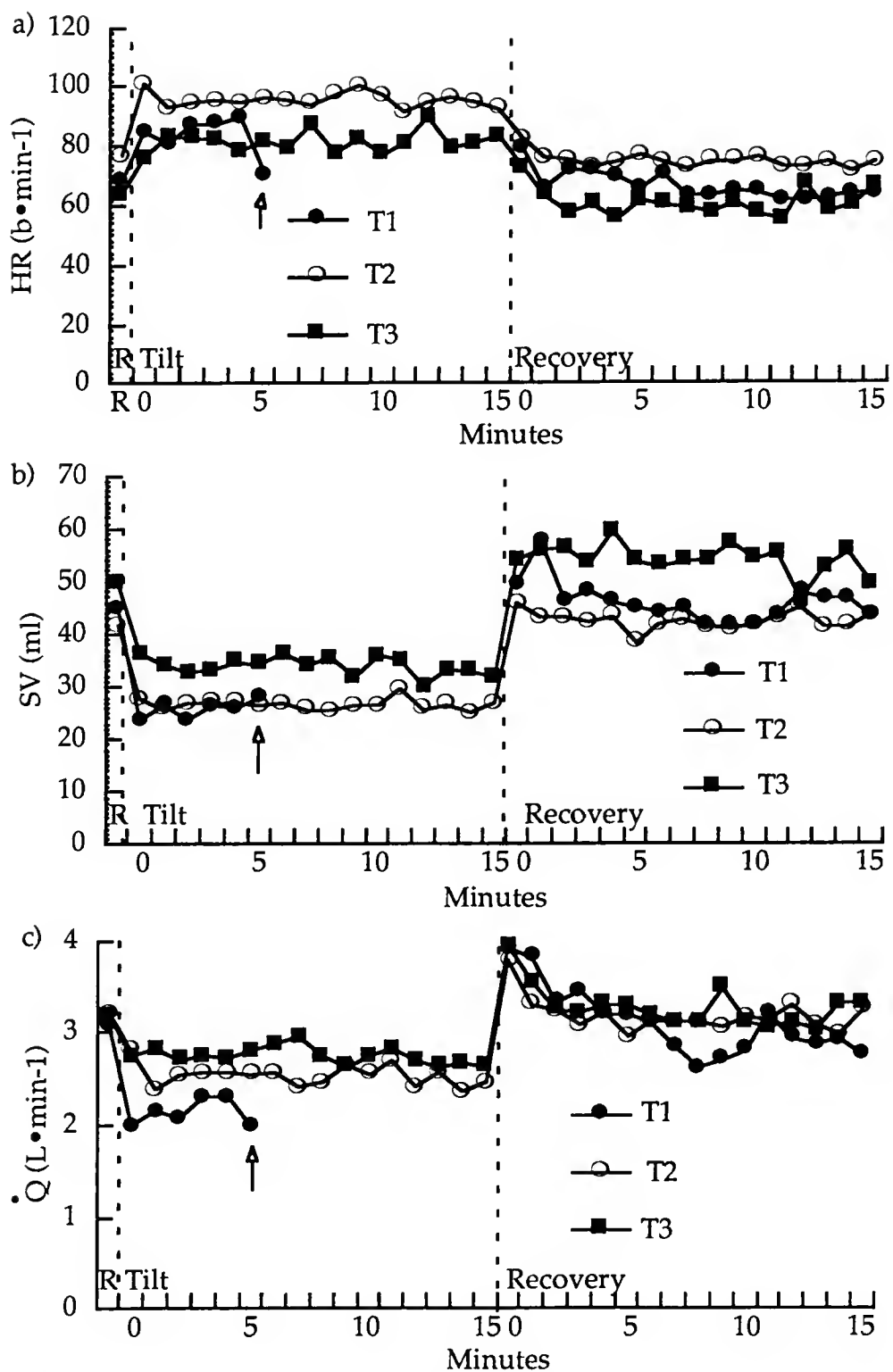
Cough #: _____

 Δ R-R: _____ Time to min. R-R: _____

Beat	R-R	Cum. time.	Beat	R-R	Cum. time.	Beat	R-R	Cum. time.
1	_____	_____	46	_____	_____	78	_____	_____
2	_____	_____	47	_____	_____	79	_____	_____
3	_____	_____	48	_____	_____	80	_____	_____
4	_____	_____	41	_____	_____	81	_____	_____
5	_____	_____	42	_____	_____	82	_____	_____
6	_____	_____	43	_____	_____	83	_____	_____
7	_____	_____	44	_____	_____	84	_____	_____
8	_____	_____	45	_____	_____	85	_____	_____
9	_____	_____	46	_____	_____	86	_____	_____
10	_____	_____	47	_____	_____	87	_____	_____
11	_____	_____	48	_____	_____	88	_____	_____
12	_____	_____	49	_____	_____	89	_____	_____
13	_____	_____	50	_____	_____	90	_____	_____
14	_____	_____	51	_____	_____	91	_____	_____
15	_____	_____	52	_____	_____	92	_____	_____
16	_____	_____	53	_____	_____	93	_____	_____
17	_____	_____	54	_____	_____	94	_____	_____
18	_____	_____	55	_____	_____	95	_____	_____
19	_____	_____	56	_____	_____	96	_____	_____
20	_____	_____	57	_____	_____	97	_____	_____
21	_____	_____	58	_____	_____	99	_____	_____
22	_____	_____	59	_____	_____	100	_____	_____
23	_____	_____	60	_____	_____	101	_____	_____
24	_____	_____	61	_____	_____	102	_____	_____
25	_____	_____	62	_____	_____	103	_____	_____
26	_____	_____	63	_____	_____	104	_____	_____
27	_____	_____	64	_____	_____	105	_____	_____
28	_____	_____	65	_____	_____	106	_____	_____
29	_____	_____	66	_____	_____	107	_____	_____
30	_____	_____	67	_____	_____	108	_____	_____
31	_____	_____	68	_____	_____	109	_____	_____
32	_____	_____	69	_____	_____	110	_____	_____
33	_____	_____	70	_____	_____	111	_____	_____
34	_____	_____	71	_____	_____	112	_____	_____
35	_____	_____	72	_____	_____	113	_____	_____
36	_____	_____	73	_____	_____	114	_____	_____
37	_____	_____	74	_____	_____	115	_____	_____
38	_____	_____	75	_____	_____	116	_____	_____
39	_____	_____	76	_____	_____	117	_____	_____
40	_____	_____	77	_____	_____	118	_____	_____

APPENDIX E

INDIVIDUAL FAINTERS' DATA



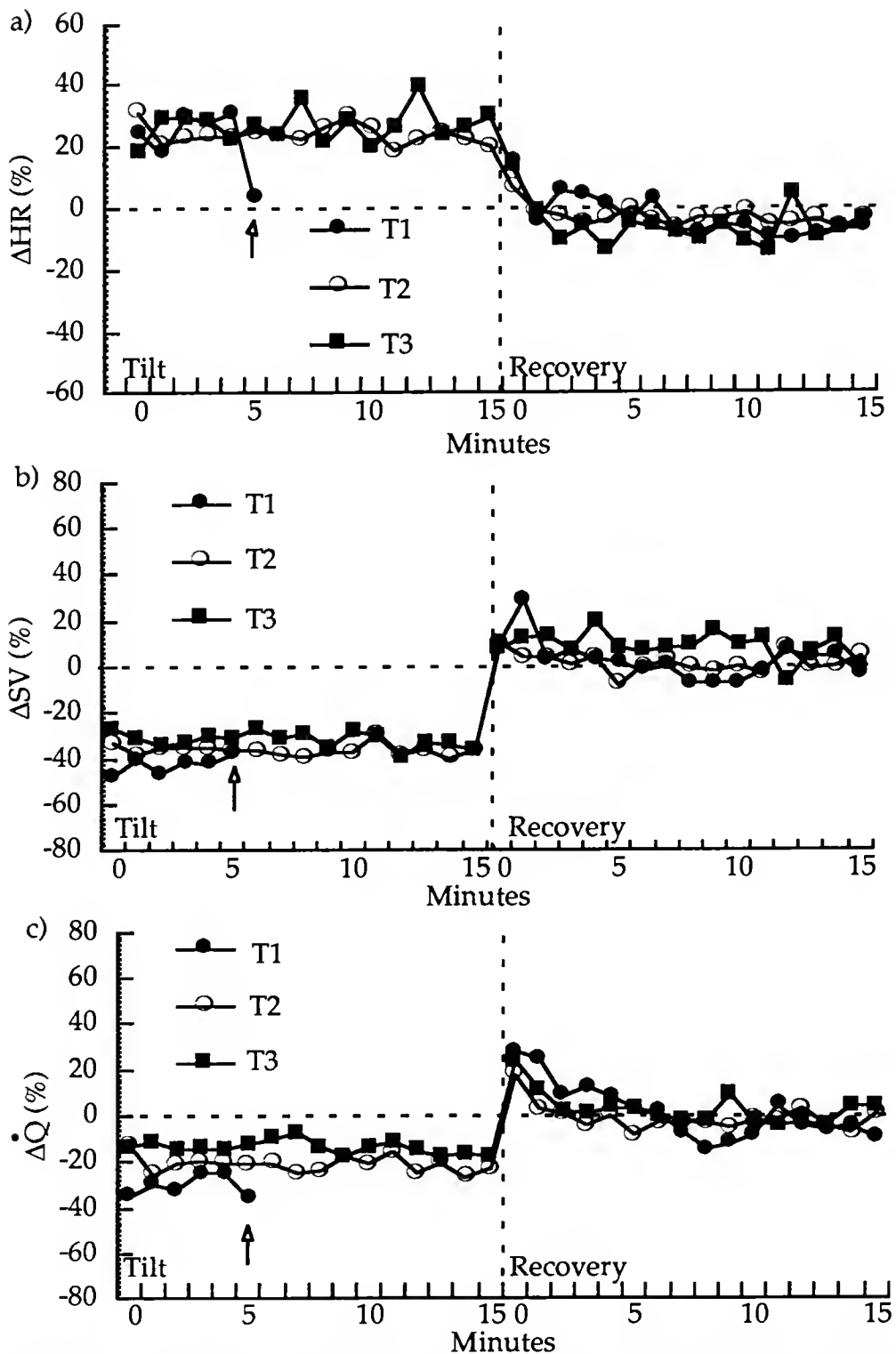


Figure E-2. Percent change (Δ) from supine rest in response to 70° head-up tilt in female fainter A before (T1), after 3 months (T2), and after 6 months (T3) of exercise training: a) heart rate (HR); b) stroke volume (SV); c) cardiac output (\dot{Q}). Arrows mark time of occurrence of presyncopal symptoms at T1.

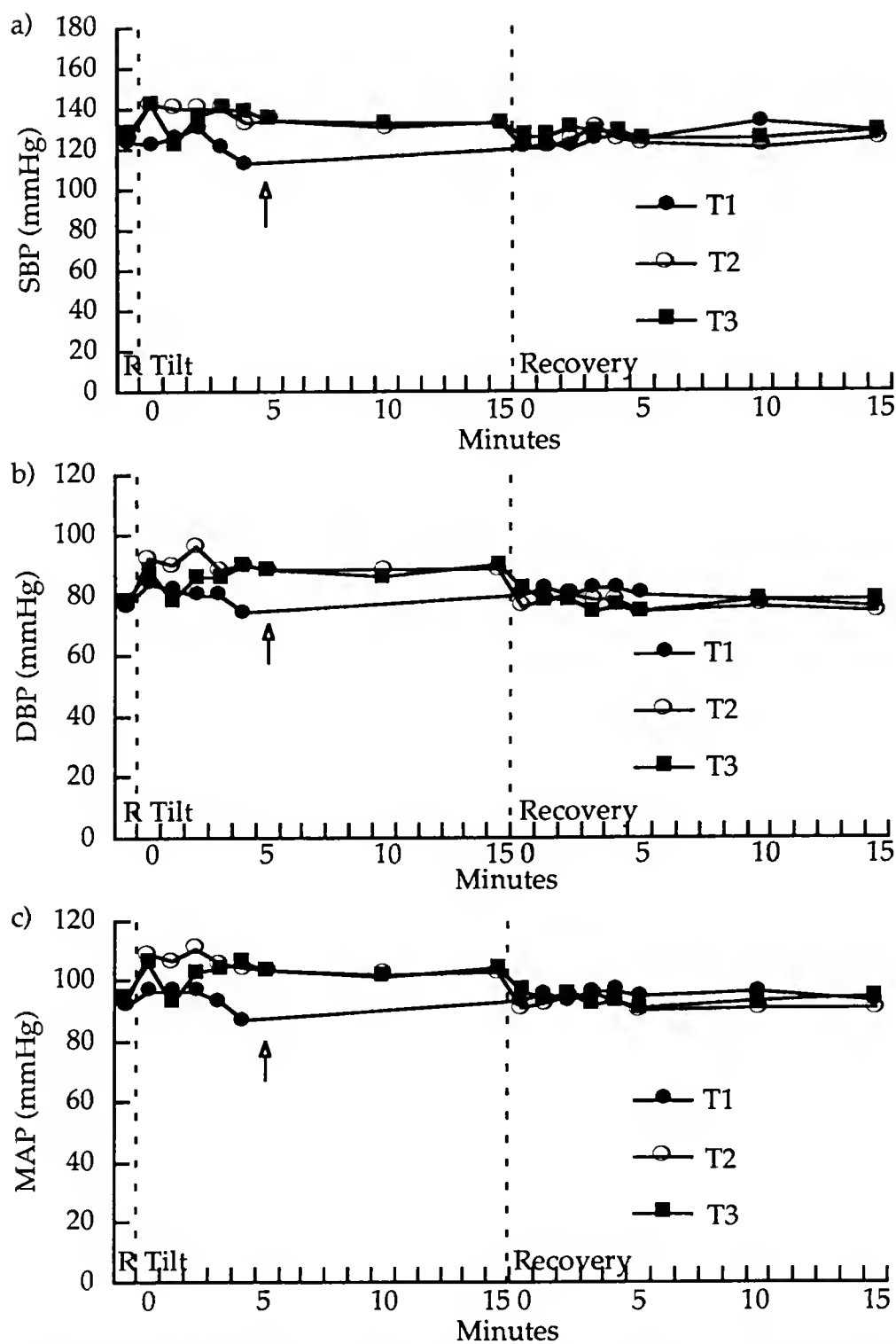


Figure E-3. Blood pressure responses of female fainter A to 70° head-up tilt before (T1), after 3 months (T2), and after 6 months (T3) of exercise training: A) systolic (SBP); b) diastolic (DBP); c) mean arterial (MAP) pressure. Arrows mark time of occurrence of presyncopal symptoms at T1. (R = Rest)

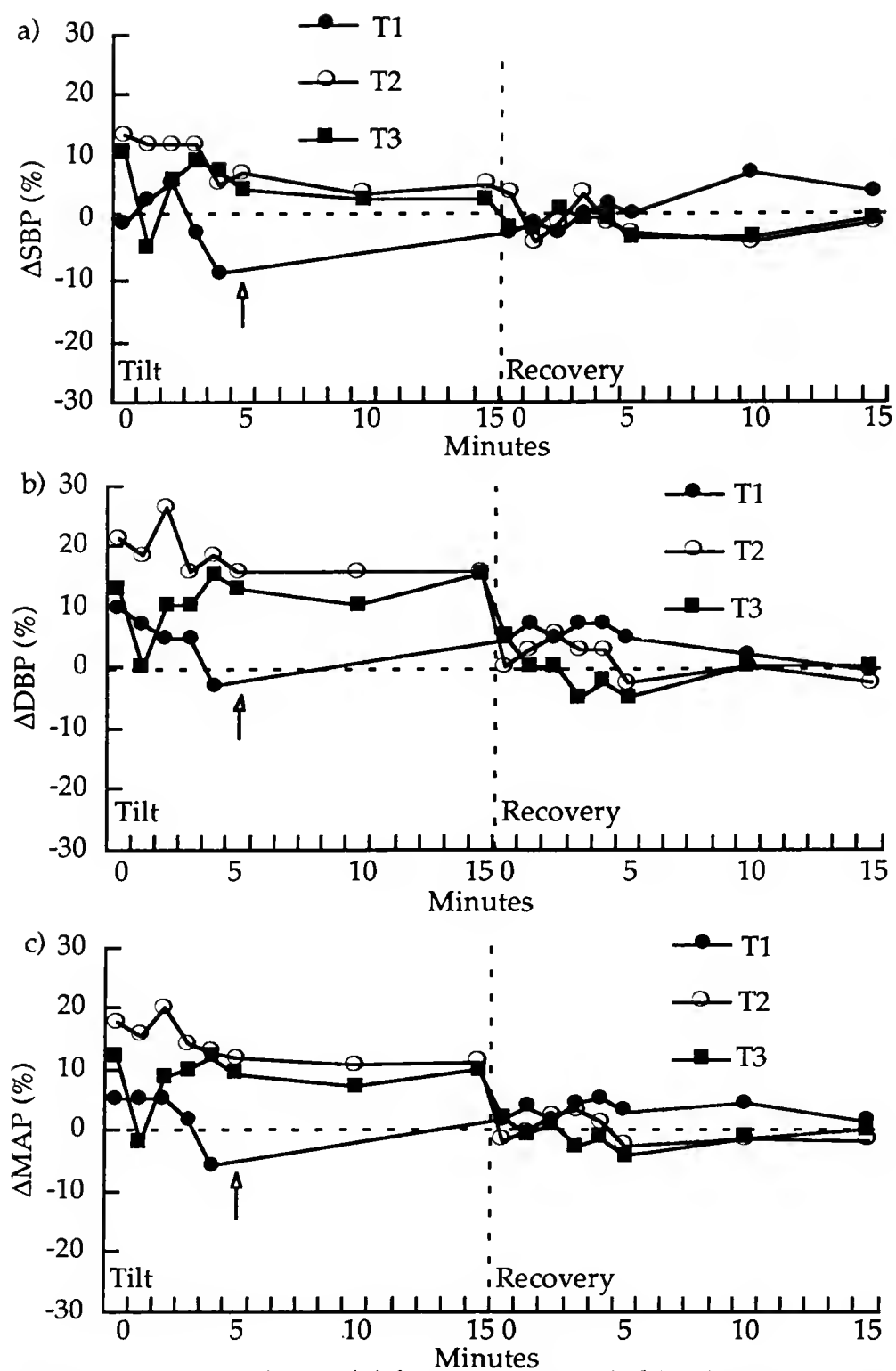
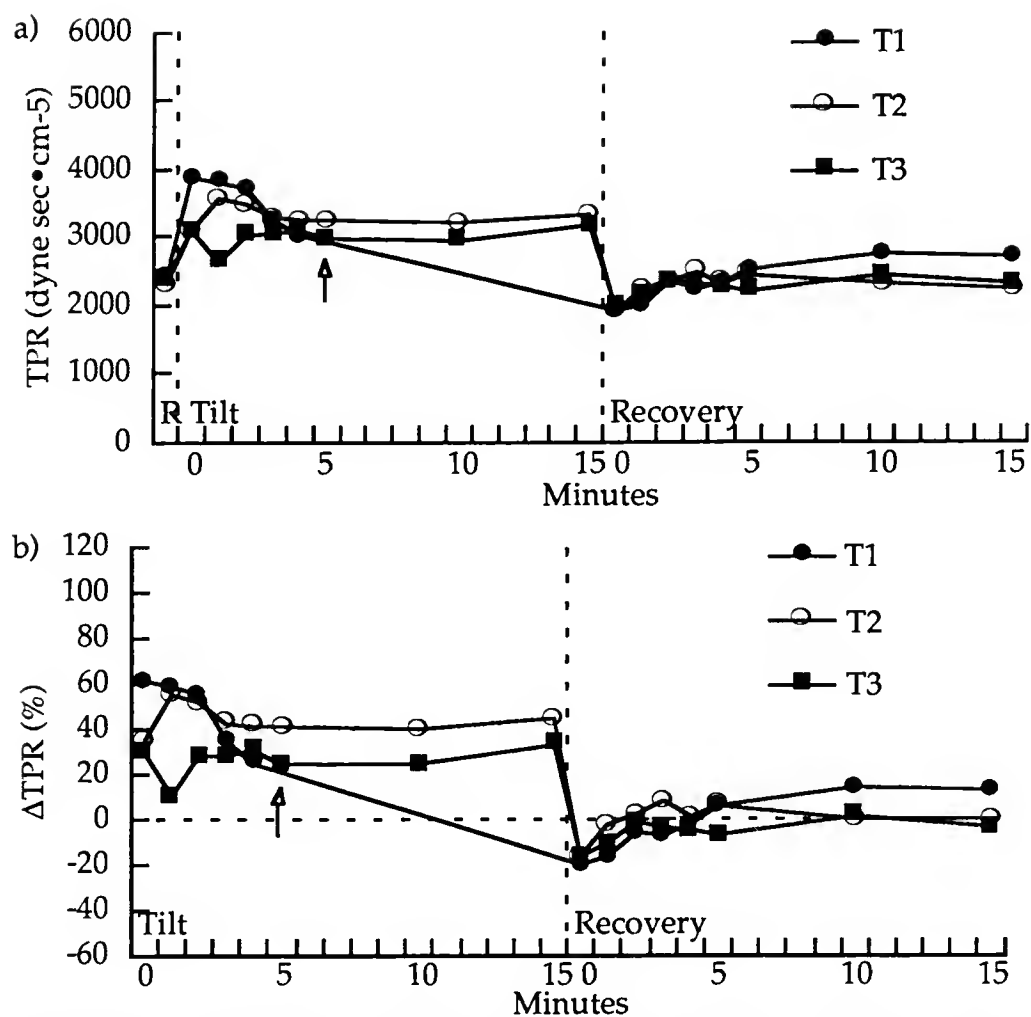


Figure E-4. Percent change (Δ) from supine rest in blood pressure response to 70° head-up tilt in female fainter A before (T1), after 3 months (T2), and after 6 months (T3) of exercise training: a) systolic (SBP); b) diastolic (DBP); c) mean arterial (MAP) pressure. Arrows mark time of occurrence of presyncopal symptoms at T1.



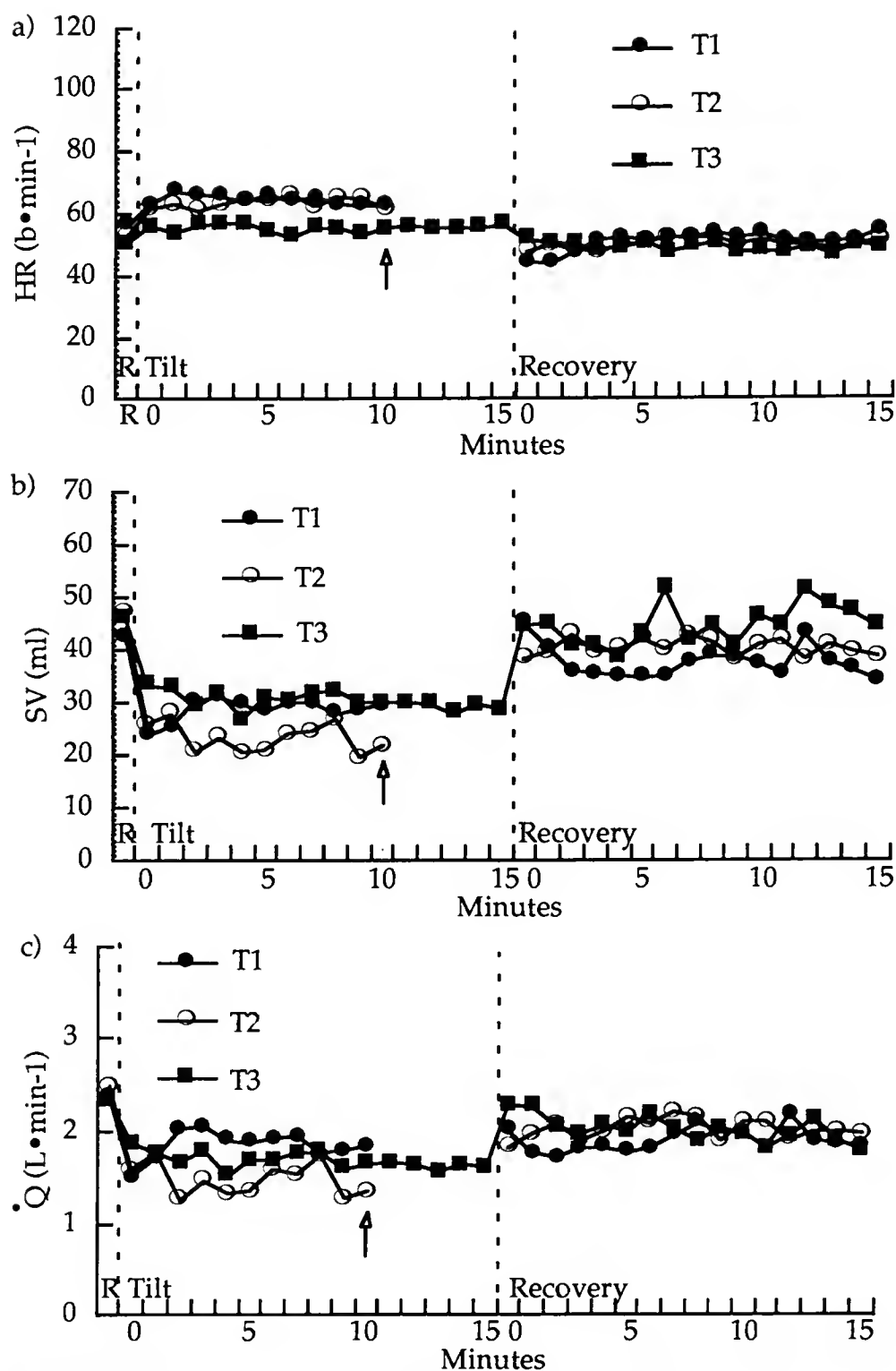


Figure E-6. Responses of female fainter B to 70° head-up tilt before (T1), after 3 months (T2), and after 6 months (T3) of exercise training: a) heart rate (HR); b) stroke volume (SV); c) cardiac output (\dot{Q}). Arrows mark time of occurrence of presyncopal symptoms at T1 and T2. (R = Rest)

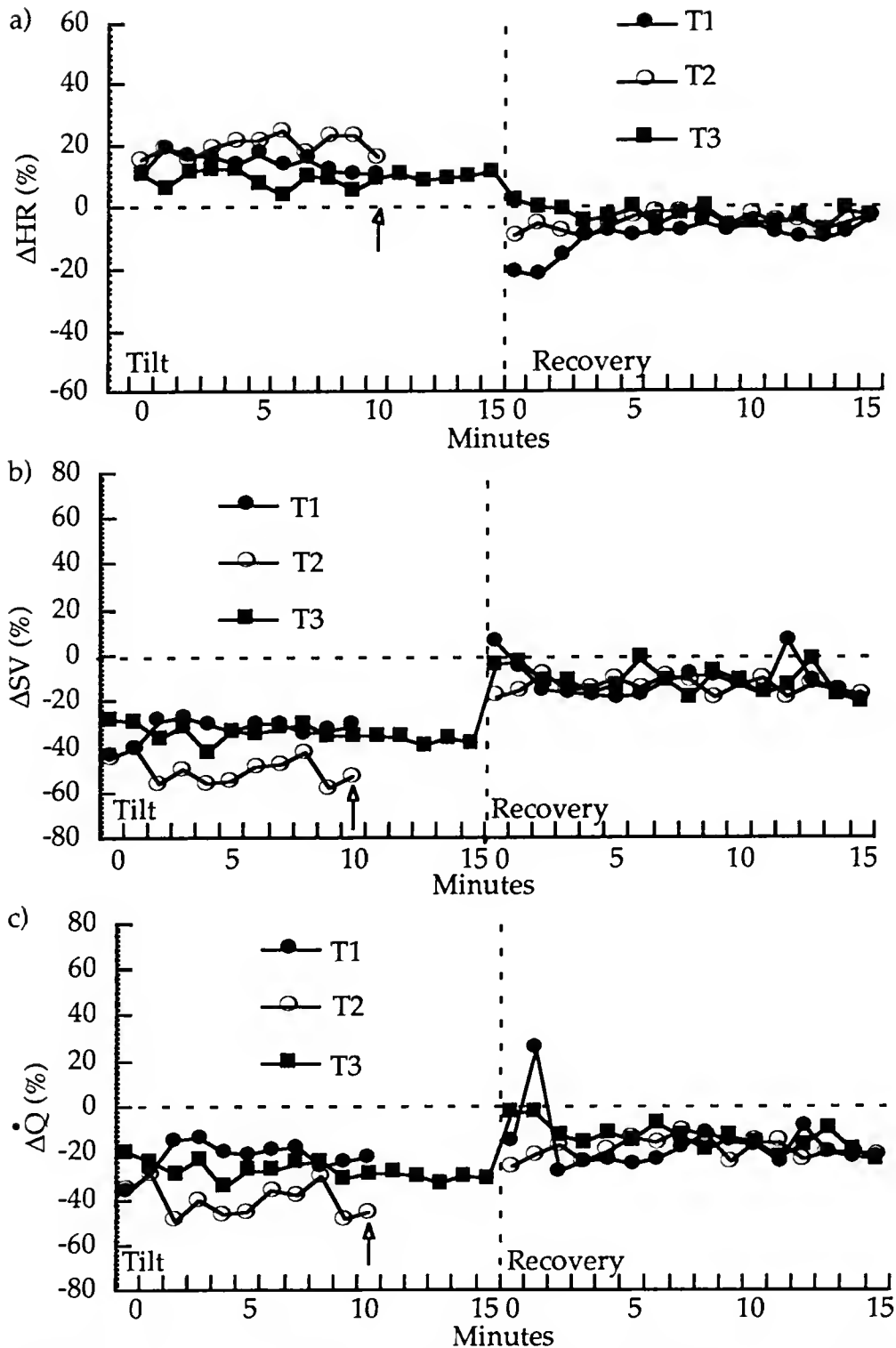


Figure E-7. Percent change (Δ) from supine rest in response to 70° head-up tilt in female fainter B before (T1), after 3 months (T2), and after 6 months (T3) of exercise training: a) heart rate (HR); b) stroke volume (SV); c) cardiac output (\dot{Q}). Arrows mark time of occurrence of presyncopal symptoms at T1 and T2.

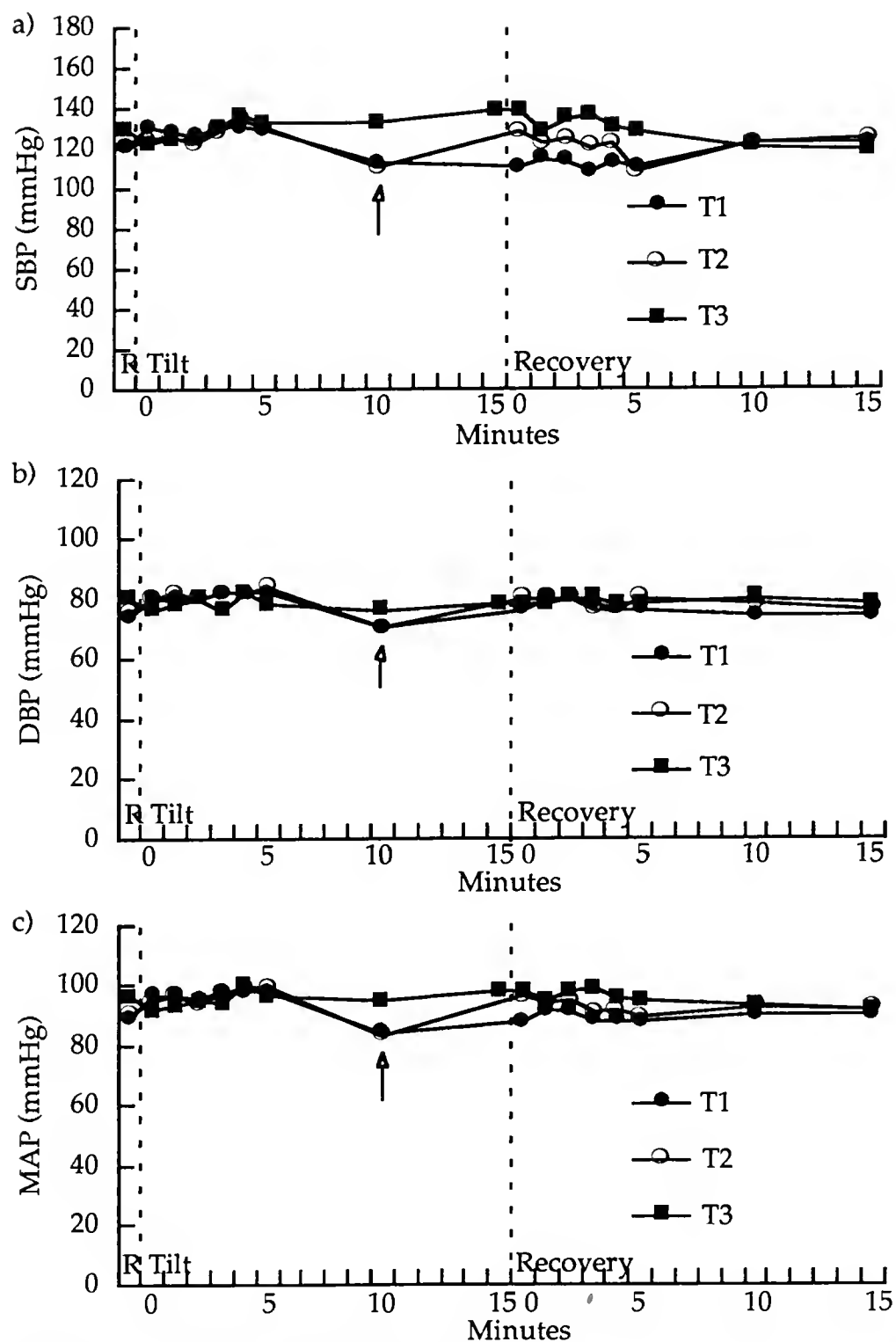


Figure E-8. Blood pressure responses of female fainter *B* to 70° head-up tilt before (T1), after 3 months (T2), and after 6 months (T3) of exercise training: A) systolic (SBP); b) diastolic (DBP); c) mean arterial (MAP) pressure. Arrows mark time of occurrence of presyncopal symptoms at T1 and T2. (R = Rest)

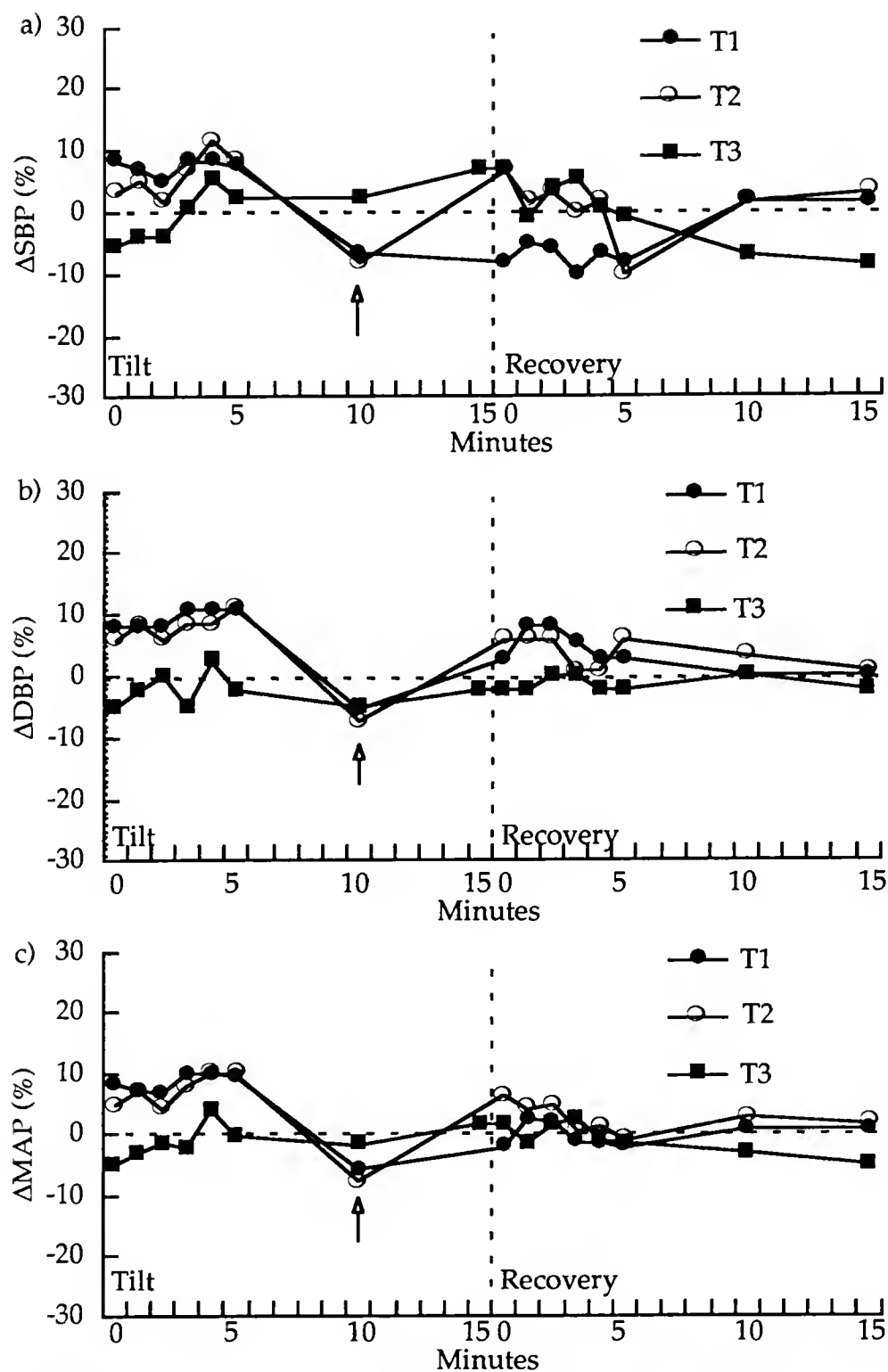


Figure E-9. Percent change (Δ) from supine rest in blood pressure response to 70° head-up tilt in female fainter B before (T1), after 3 months (T2), and after 6 months (T3) of exercise training: a) systolic (SBP); b) diastolic (DBP); c) mean arterial (MAP) pressure. Arrows mark time of occurrence of presyncopal symptoms at T1 and T2.

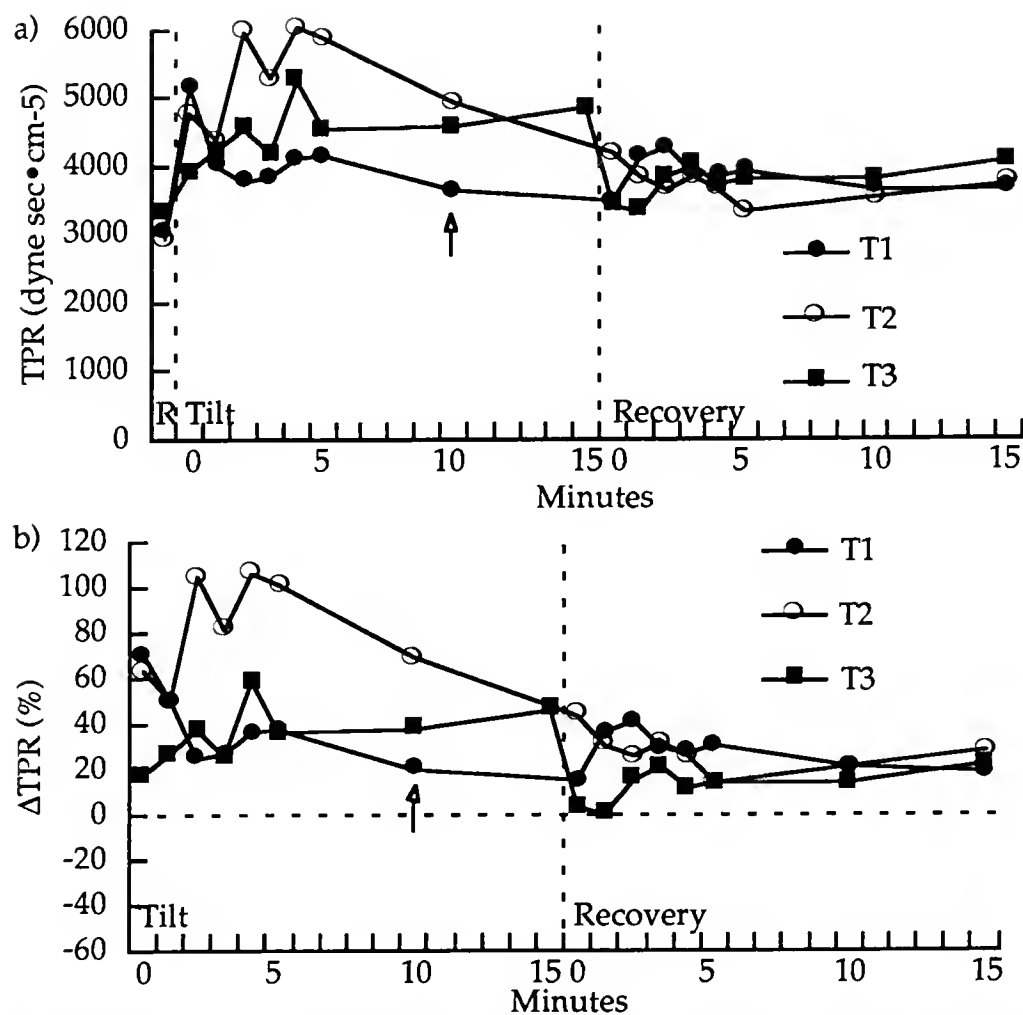


Figure E-10. Total peripheral resistance (TPR) response of female fainter *B* to 70° head-up tilt before (T1), after 3 months (T2), and after 6 months (T3) of exercise training: a) absolute response; b) percent change (Δ) from supine rest. Arrows indicate time of occurrence of presyncopal symptoms at T1 and T2.

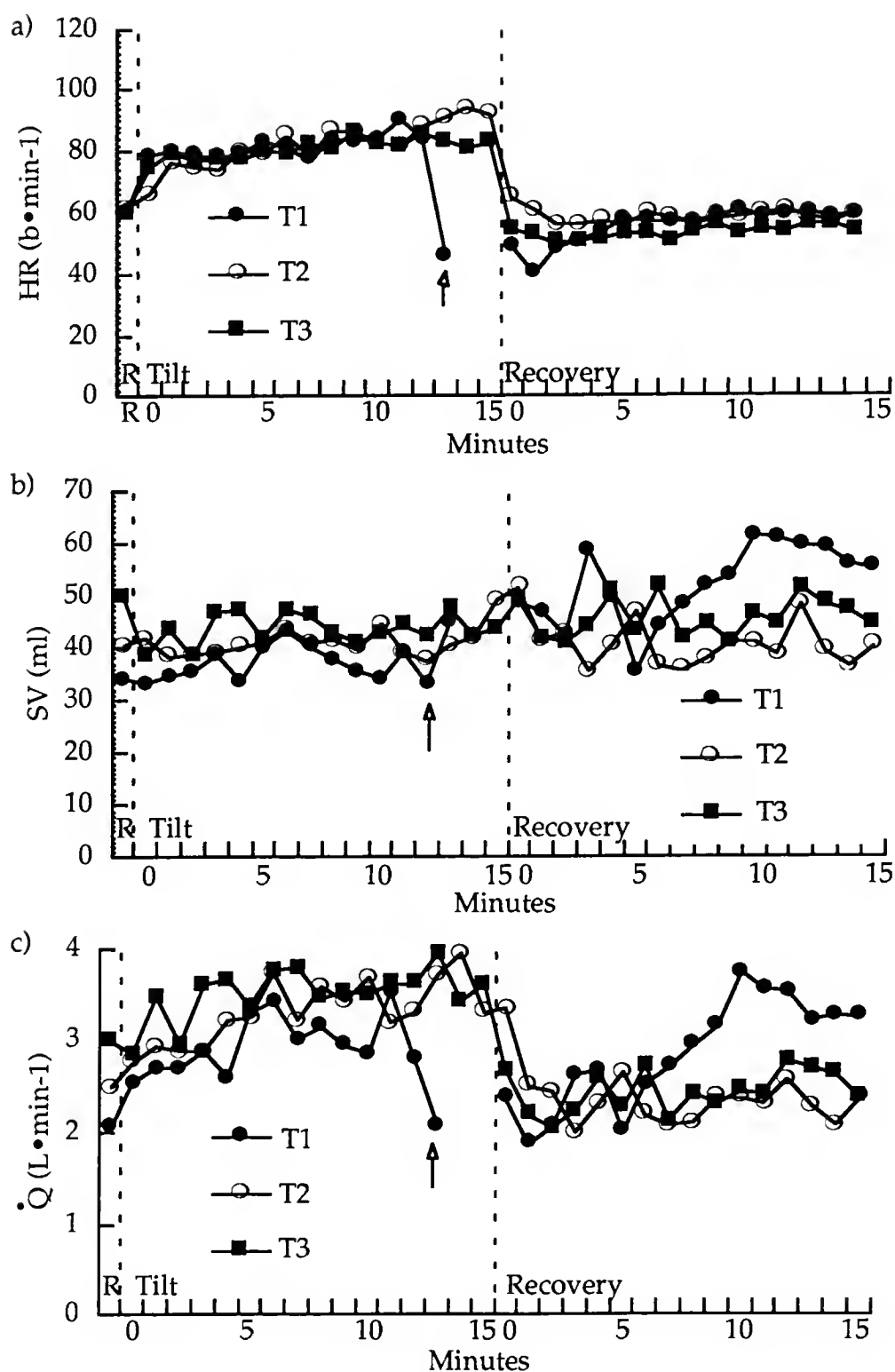


Figure E-11. Responses of male fainter A to 70° head-up tilt before (T1), after 3 months (T2), and after 6 months (T3) of exercise training: a) heart rate (HR); b) stroke volume (SV); c) cardiac output (\dot{Q}). Arrows mark time of occurrence of presyncopal symptoms at T1. (R = Rest)

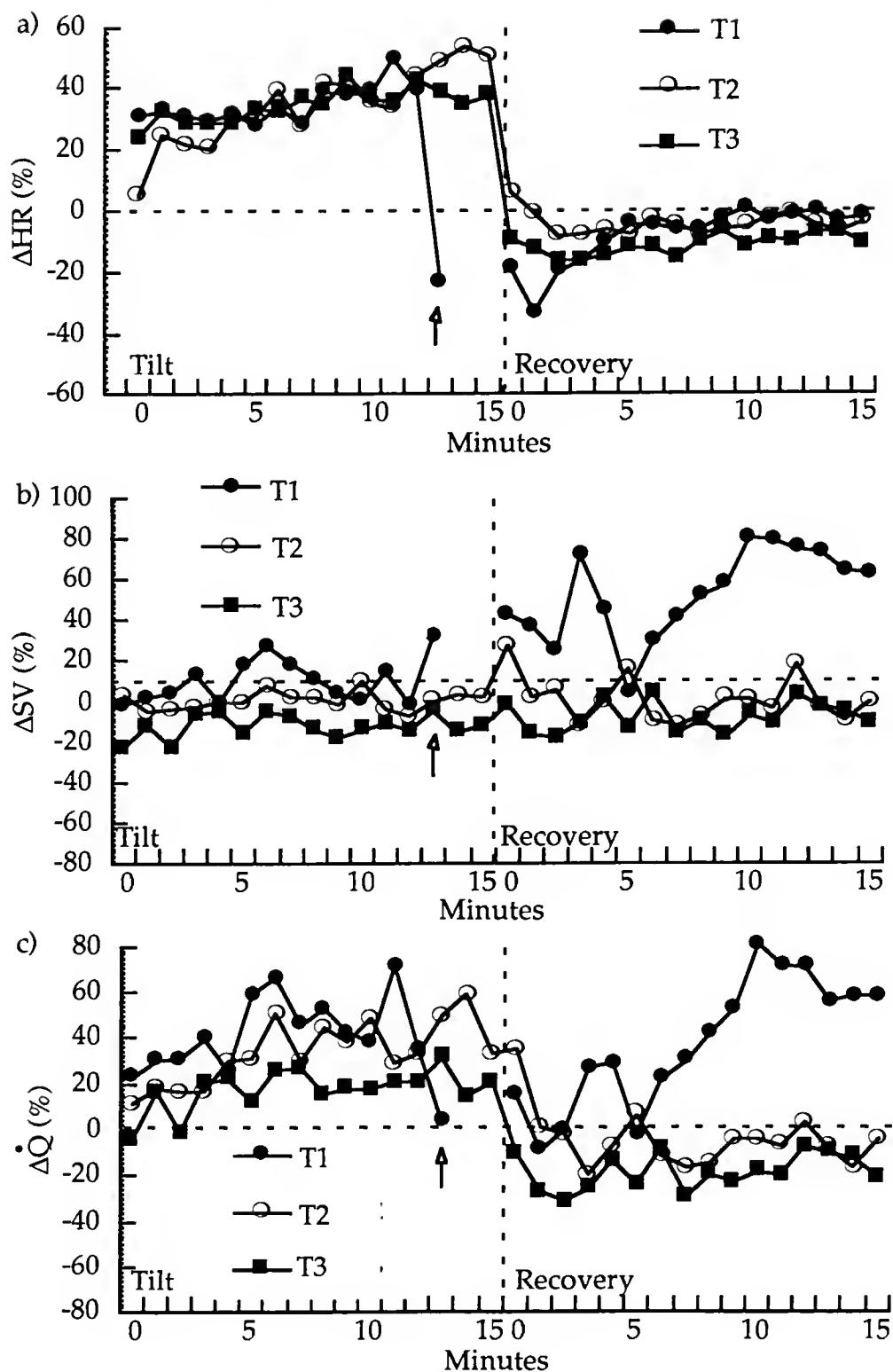


Figure E-12. Percent change (Δ) from supine rest in response to 70° head-up tilt in male fainter A before (T1), after 3 months (T2), and after 6 months (T3) of exercise training: a) heart rate (HR); b) stroke volume (SV); c) cardiac output (\dot{Q}). Arrows mark time of occurrence of presyncopal symptoms at T1.

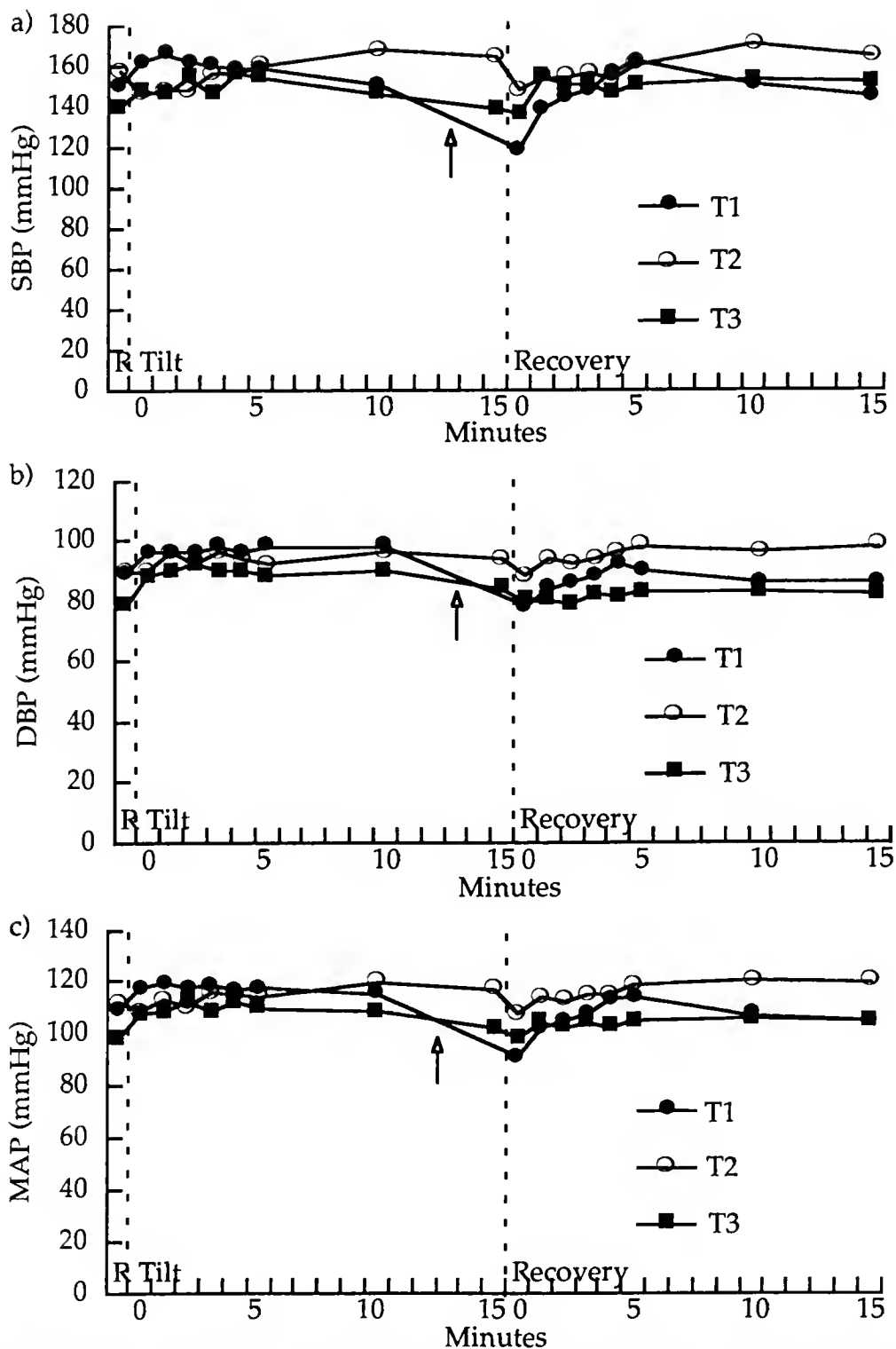


Figure E-13. Blood pressure responses of male fainter A to 70° head-up tilt before (T1), after 3 months (T2), and after 6 months (T3) of exercise training: A) systolic (SBP); b) diastolic (DBP); c) mean arterial (MAP) pressure. Arrows mark time of occurrence of presyncopal symptoms at T1. (R = Rest)

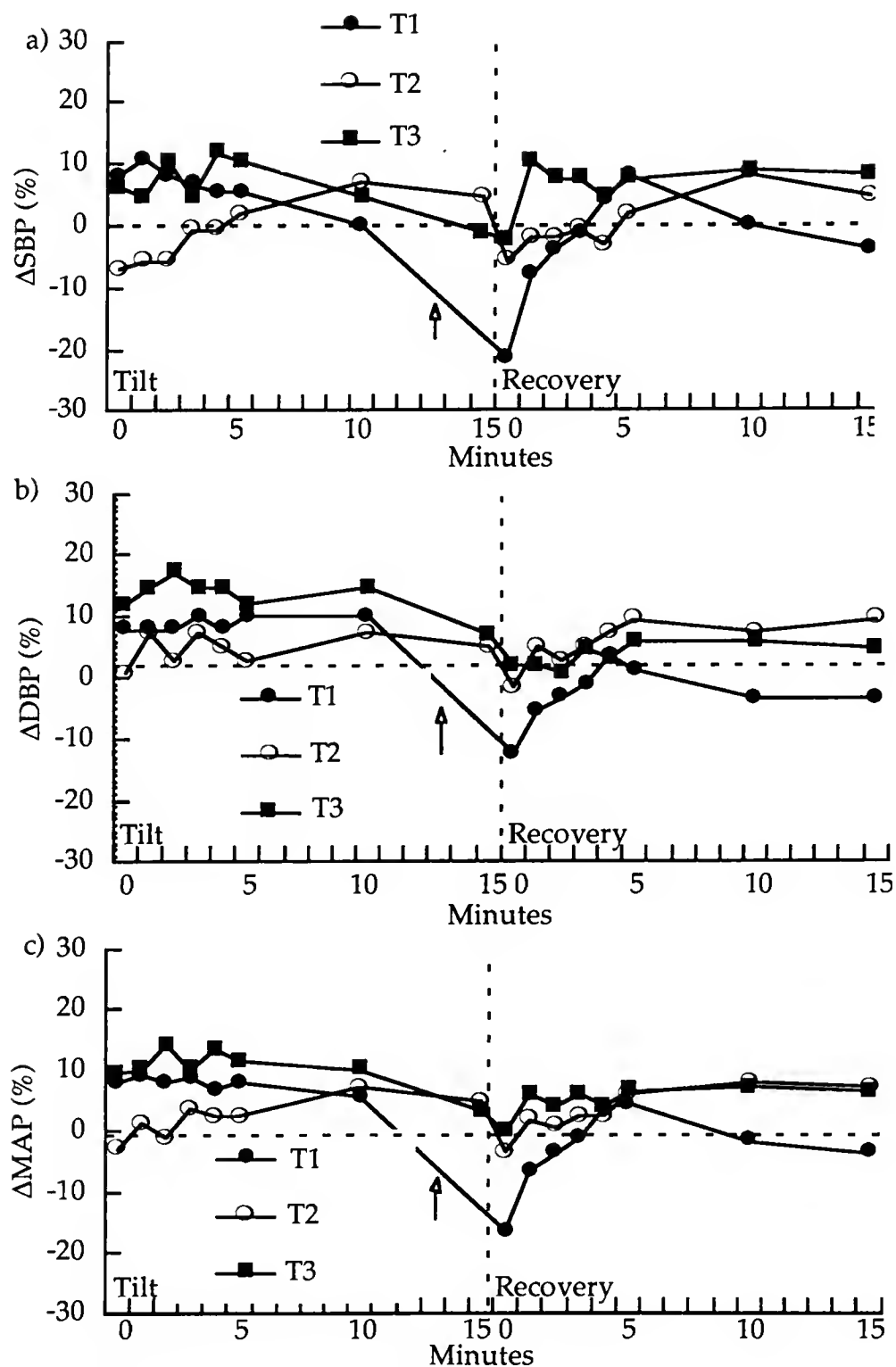


Figure E-14. Percent change (Δ) from supine rest in blood pressure response to 70° head-up tilt in male fainter A before (T1), after 3 months (T2), and after 6 months (T3) of exercise training: a) systolic (SBP); b) diastolic (DBP); c) mean arterial (MAP) pressure. Arrows mark time of occurrence of presyncopal symptoms at T1.

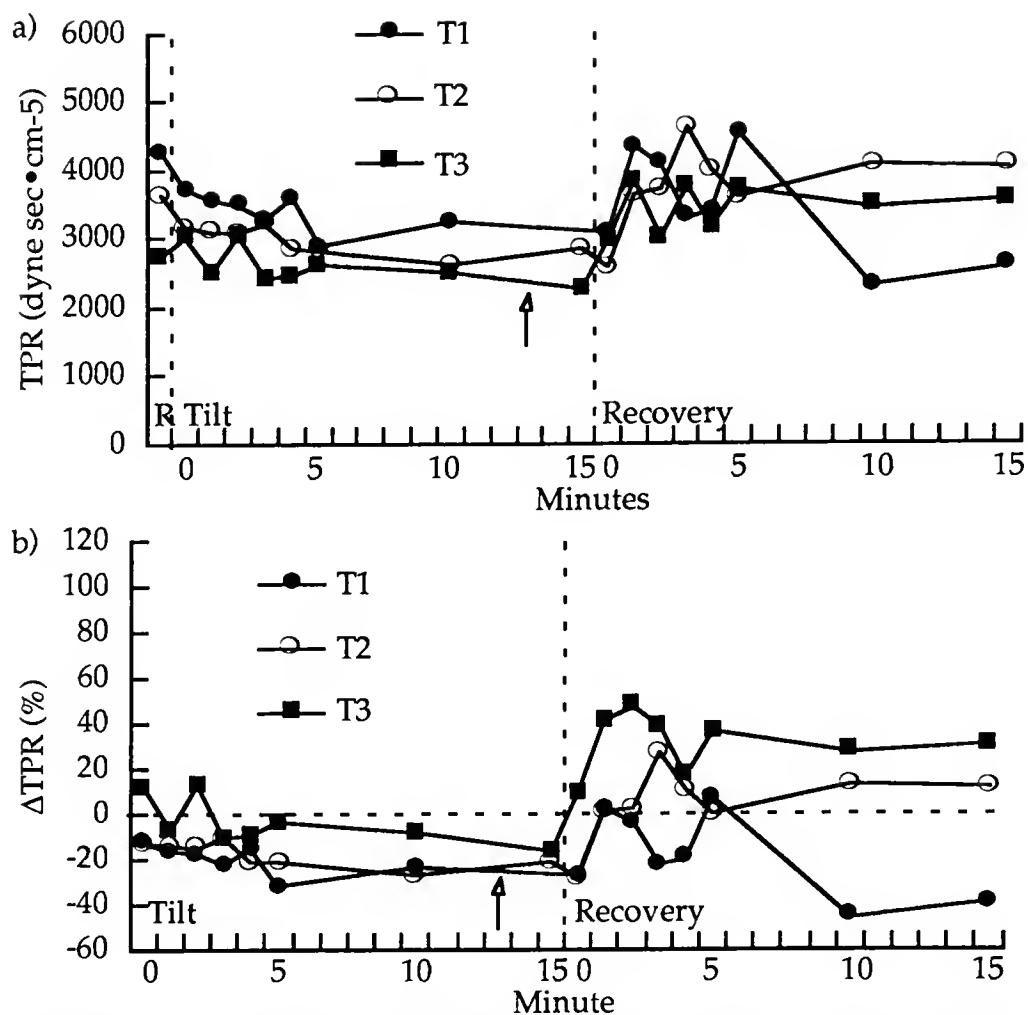


Figure E-15. Total peripheral resistance (TPR) response of male fainter A to 70° head-up tilt before (T1), after 3 months (T2), and after 6 months (T3) of exercise training: a) absolute response; b) percent change (Δ) from supine rest. Arrows indicate time of occurrence of presyncopal symptoms at T1.

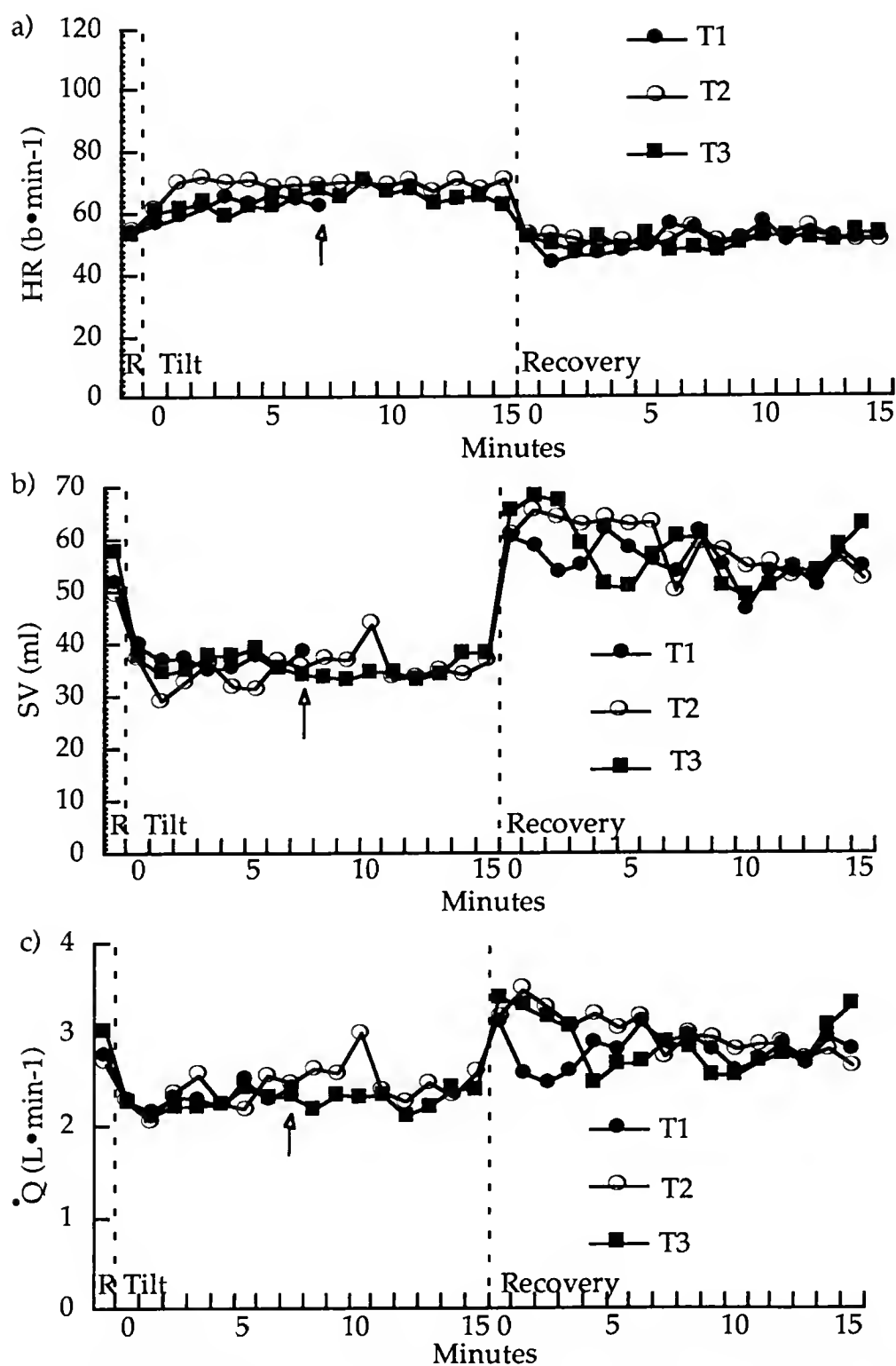


Figure E-16. Responses of male fainter B to 70° head-up tilt before (T1), after 3 months (T2), and after 6 months (T3) of exercise training: a) heart rate (HR); b) stroke volume (SV); c) cardiac output (\dot{Q}). Arrows mark time of occurrence of presyncopal symptoms at T1. (R = Rest)

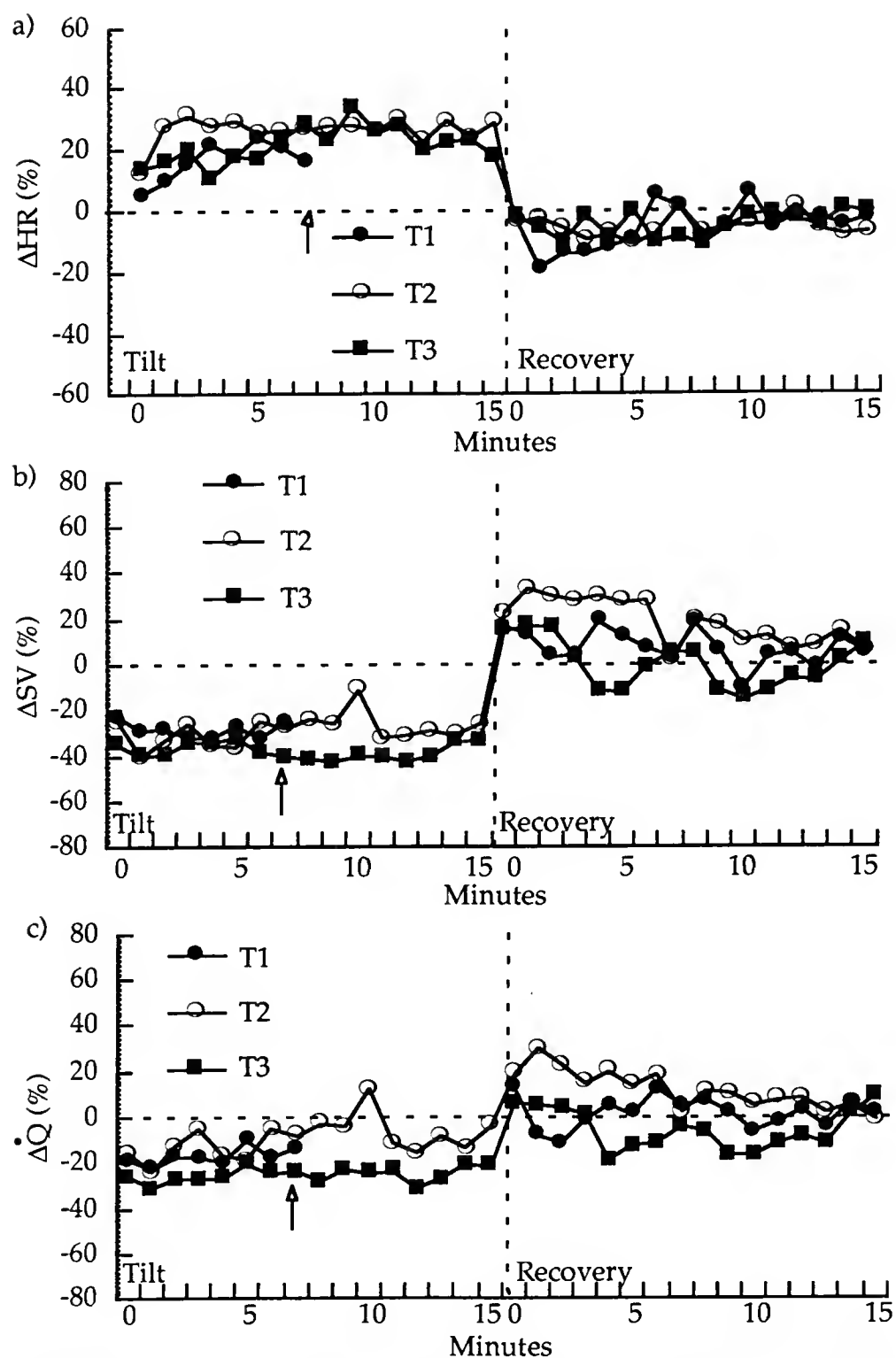


Figure E-17. Percent change (Δ) from supine rest in response to 70° head-up tilt in male fainter B before (T1), after 3 months (T2), and after 6 months (T3) of exercise training: a) heart rate (HR); b) stroke volume (SV); c) cardiac output (\dot{Q}). Arrows mark time of occurrence of presyncopal symptoms at T1.

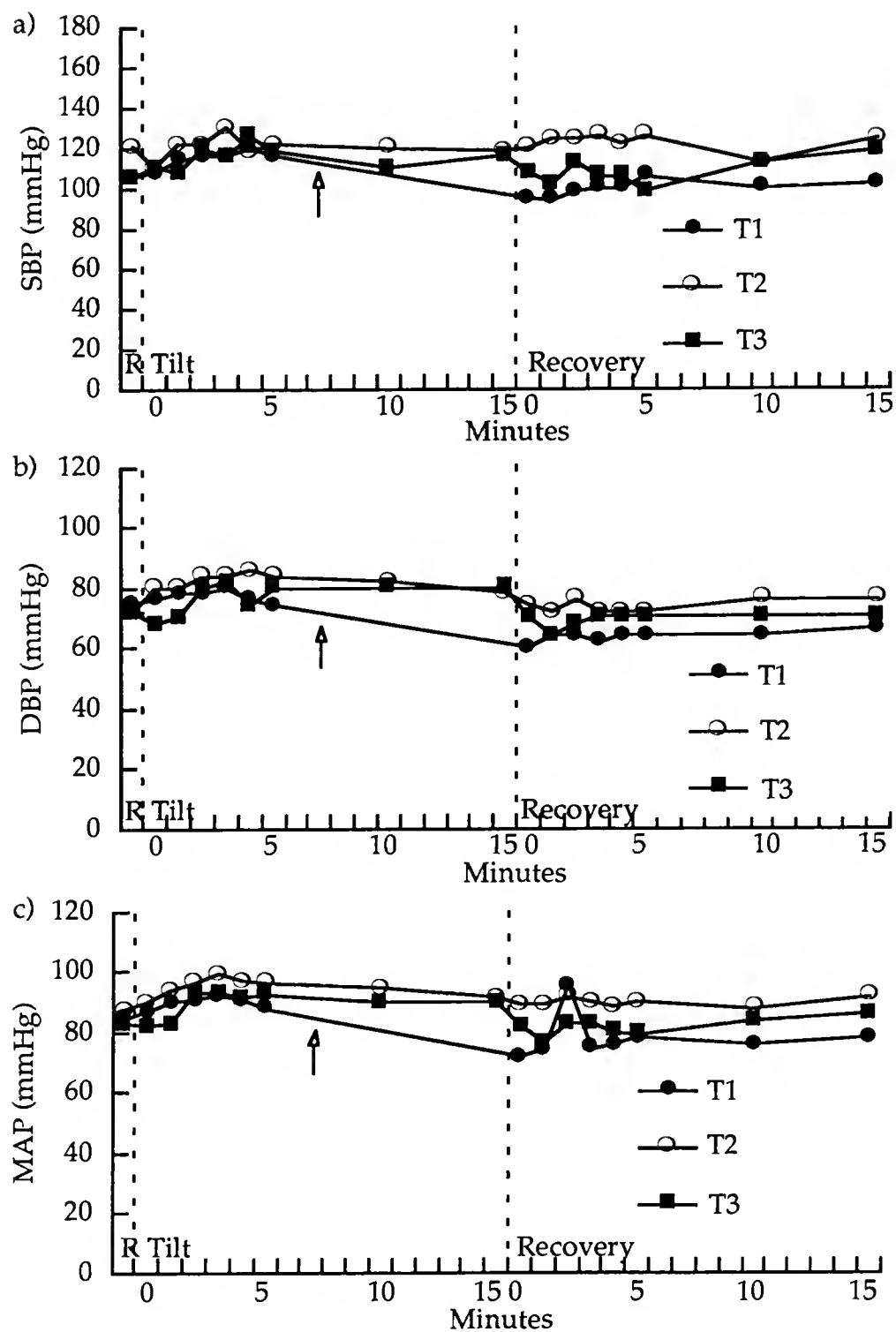


Figure E-18. Blood pressure responses of male fainter *B* to 70° head-up tilt before (T1), after 3 months (T2), and after 6 months (T3) of exercise training: A) systolic (SBP); b) diastolic (DBP); c) mean arterial (MAP) pressure. Arrows mark time of occurrence of presyncopal symptoms at T1. (R = Rest)

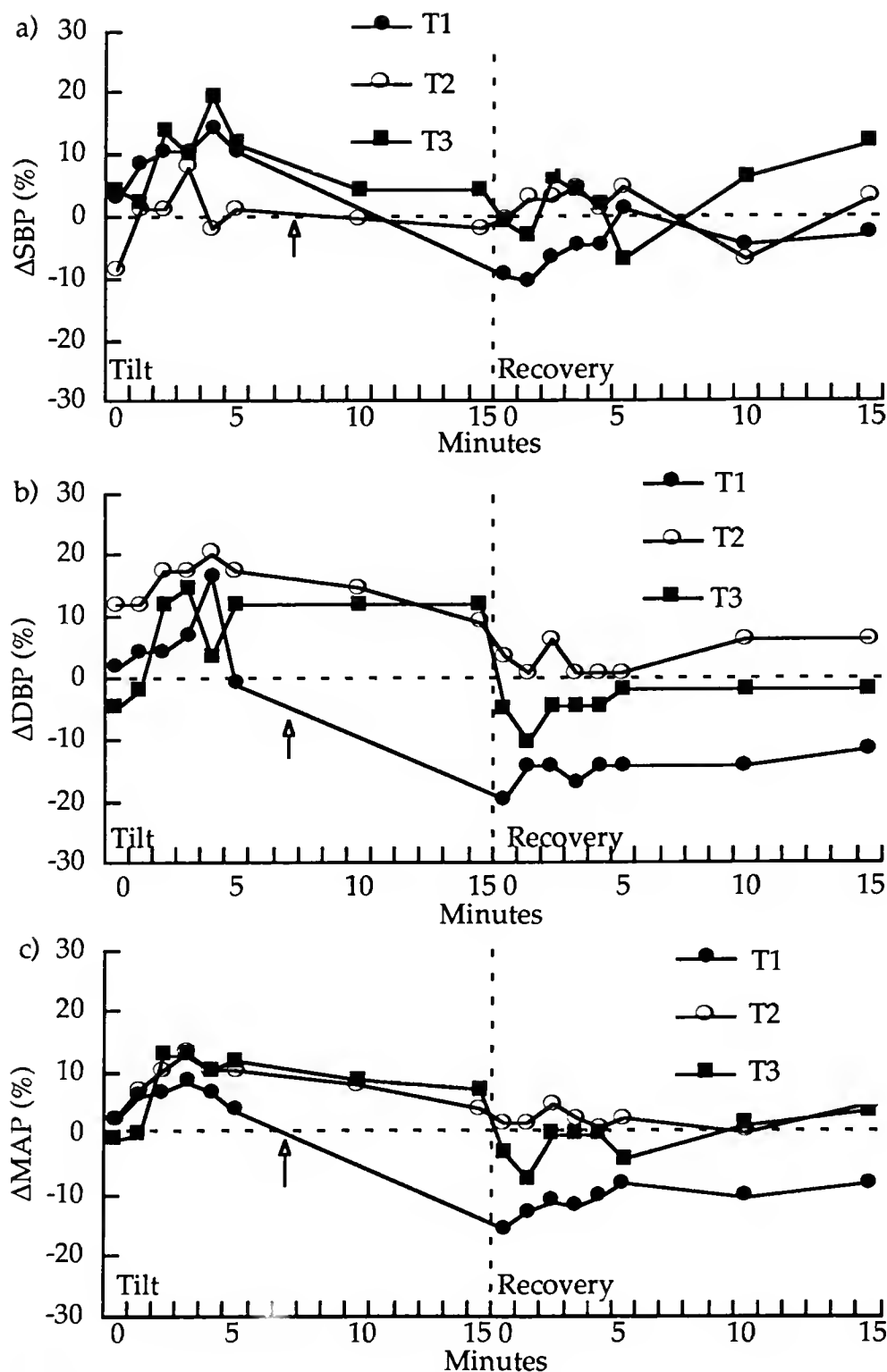


Figure E-19. Percent change (Δ) from supine rest in blood pressure response to 70° head-up tilt in male fainter B before (T1), after 3 months (T2), and after 6 months (T3) of exercise training: a) systolic (SBP); b) diastolic (DBP); c) mean arterial (MAP) pressure. Arrows mark time of occurrence of presyncopal symptoms at T1.

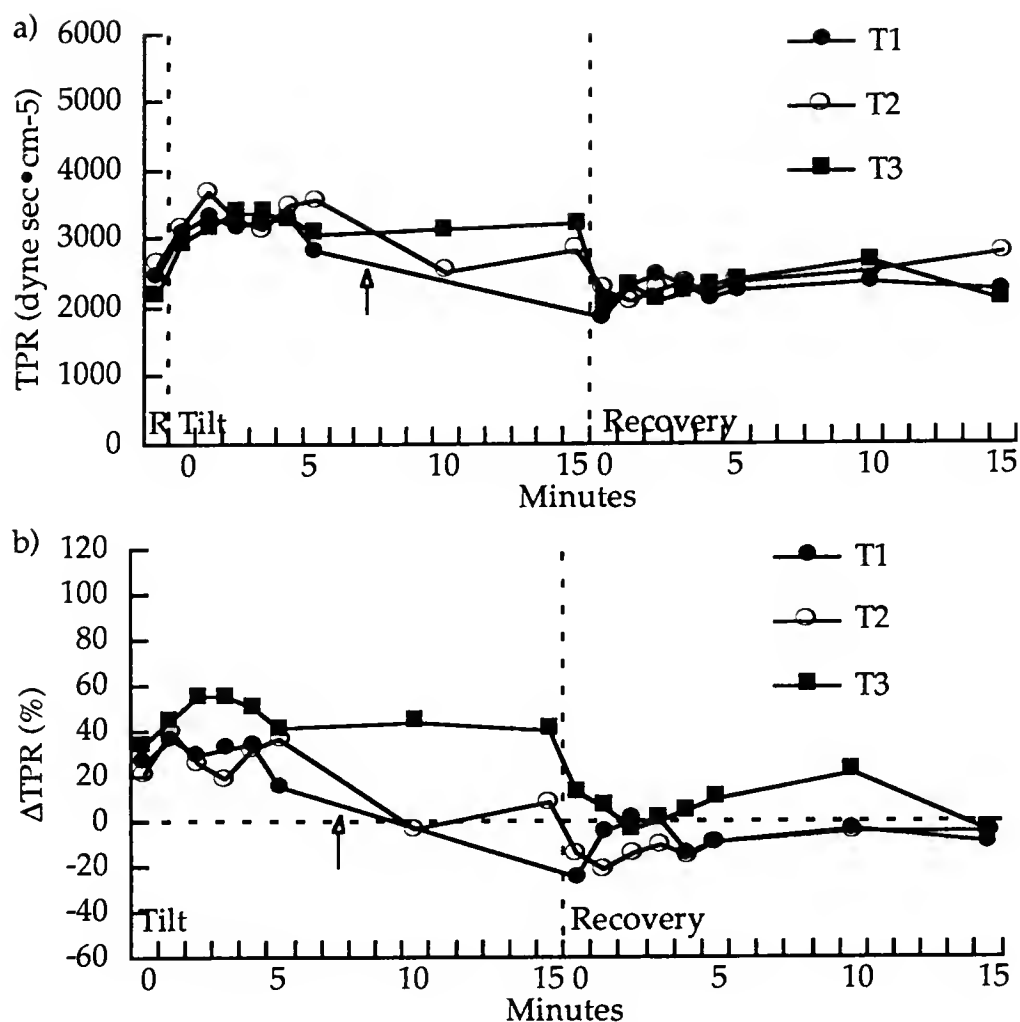


Figure E-20. Total peripheral resistance (TPR) response of male fainter B to 70° head-up tilt before (T1), after 3 months (T2), and after 6 months (T3) of exercise training: a) absolute response; b) percent change (Δ) from supine rest. Arrows indicate time of occurrence of presyncopal symptoms at T1.

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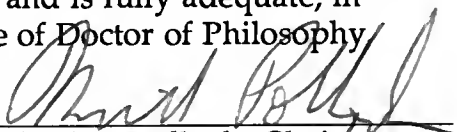
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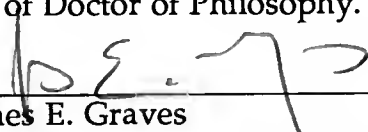
BIOGRAPHICAL SKETCH

Joan F. Carroll received a Bachelor of Arts degree from the State University of New York in Binghamton in 1975. She received her Master of Arts in Physical Education at the University of Florida in 1984. After four years of teaching at the University of Florida, she continued her studies toward a Ph.D. degree at the University of Florida. She will also earn a Certificate in Gerontology upon graduation. During her four years of study for a Ph.D., she has worked on two research projects involving cardiovascular and strength training for elderly men and women. She has also been involved in research documenting injuries with training in the elderly and the use of ultrasound in the prediction of body composition. Upon graduation, she wishes to pursue a career in teaching and research in a university setting.

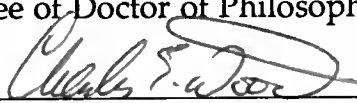
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Michael L. Pollock, Chairman
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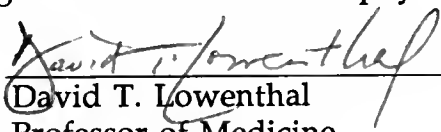
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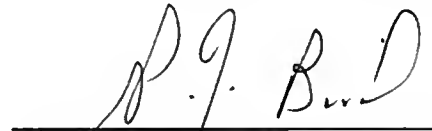


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This dissertation was submitted to the Graduate Faculty of the College of Health and Human Performance and to the Graduate School and was accepted as partial fulfillment of the requirements for the degree of Doctor of Philosophy.

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